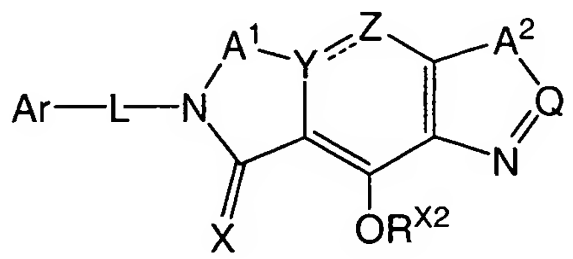
Amendments to the Claims

1. (Currently amended): A compound having the structure:

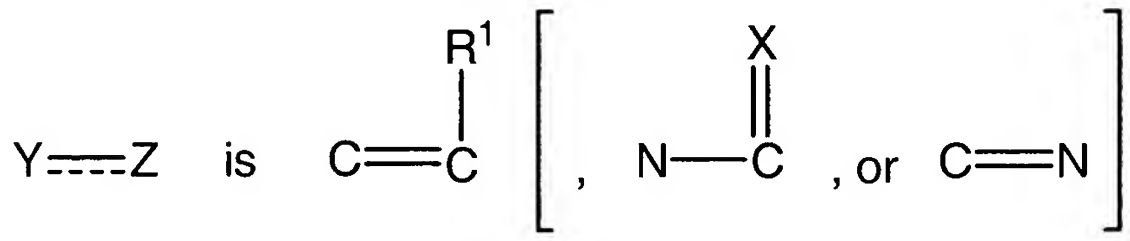


wherein:

A^1 [and A^2 are] is independently selected from [O, S, NR,] $C(R^2)_2$, CR^2OR, $CR^2OC(=O)R$, C(=O), C(=S), CR^2SR, and C(=NR),

A^2 is independently selected from $C(R^2)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$, [$C(R^2)_2$–O, NR–$C(R^3)_2$, N=$C(R^3)$, N=N, SO_2–NR,] and C(=O)$C(R^3)_2$, [C(=O)NR, $C(R^2)_2$–$C(R^3)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$–$C(R^3)_2$, $C(R^2)$C(=O)NR, $C(R^2)$C(=S)NR, $C(R^2)$=N–$C(R^3)_2$, $C(R^2)$=N–NR, and N=$C(R^3)$–NR];

Q is [N, $^+$NR, or] CR^4;

Y=Z is 

;

L is selected from a bond, O, S, S–S, S(=O), $S(=O)_2$, $S(=O)_2NR$, NR, N–OR, C_1–C_{12} alkylene, C_1–C_{12} substituted alkylene, C_2–C_{12} alkenylene, C_2–C_{12} substituted alkenylene, C_2–C_{12} alkynylene, C_2–C_{12} substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), $C(=O)NH(CH_2)_n$, or $(CH_2CH_2O)_n$, where n [may be] is optionally 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N–OR, $N–NR_2$, $N–CR_2OR$ and $N–CR_2NR_2$;

Ar is selected from (a) a C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

[R^1,] R^2, R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $–NH_2$, $–NH_3^+$, –NHR, $–NR_2$, $–NR_3^+$, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7

membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1–C_8 alkoxy, C_1–C_8 trifluoroalkyl, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

when taken together on a single carbon, two R^2 or two R^3 may form a spiro ring; [and]

R^1 is independently selected from CR_3, $NRSO_2R$, $OC(=O)NR_2$ $OC(=O)R$, SR, H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, $-NHR$, $-NR_2$, $-NR_3^+$, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1–C_8 alkoxy, C_1–C_8 trifluoroalkyl, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

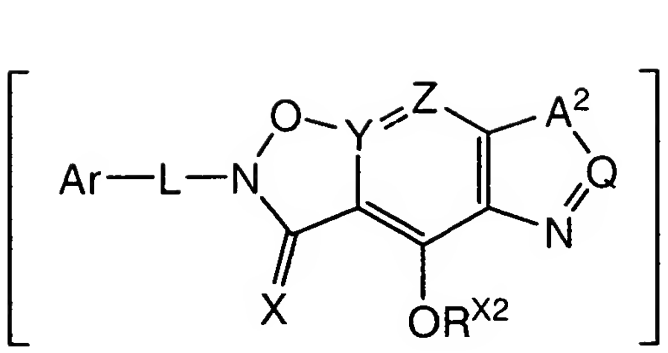
R is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

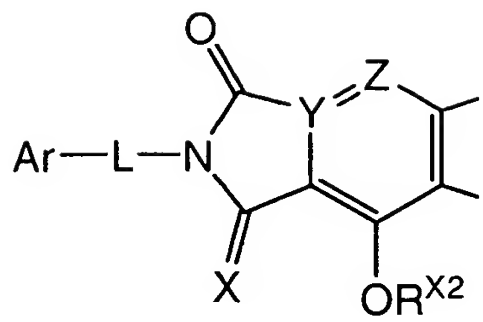
R^{X2} is independently selected from H, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, [a prodrug, a pharmaceutically acceptable prodrug,] a prodrug moiety, and a protecting group[, and a phosphonate prodrug moiety];

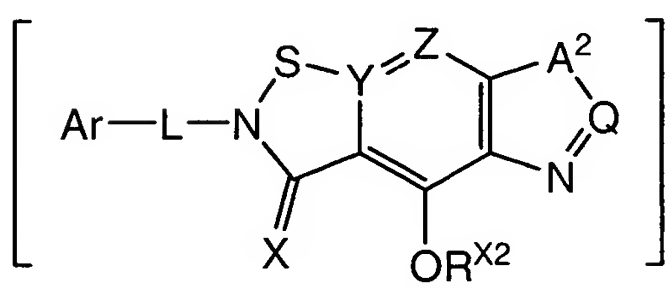
and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof;

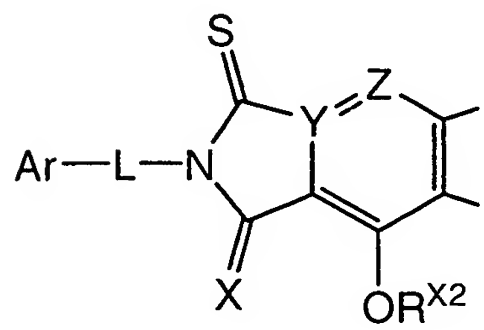
with the proviso that when Y=Z is C=C(OH), X is O, A^1 is C(=O), A^2 is $C(R^2)=C(R^3)$, and Q is CH, then L is not a bond.

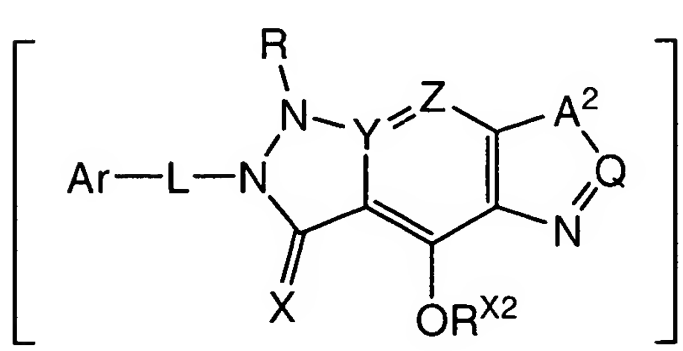
2. (Currently amended): A compound of claim 1 selected from the structures:

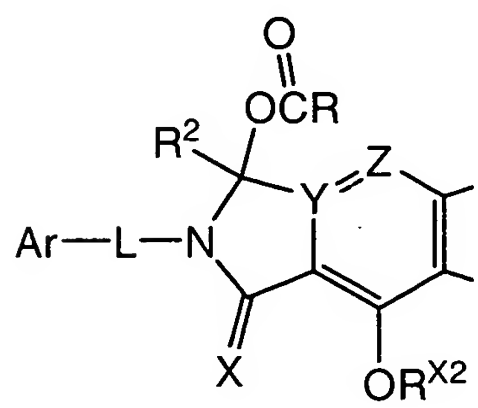


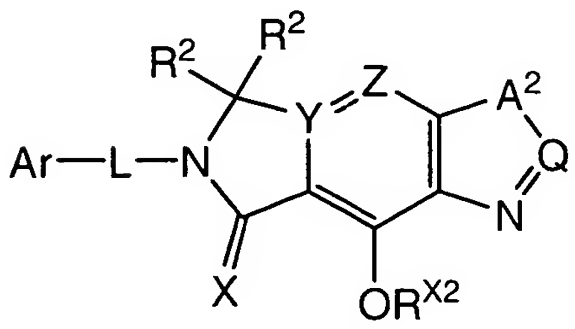


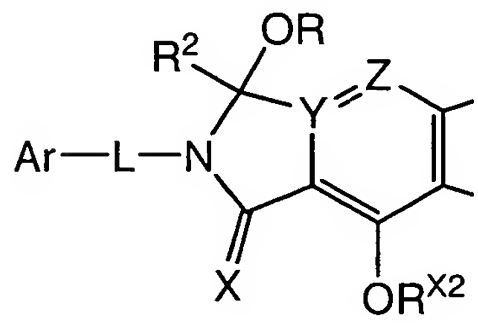


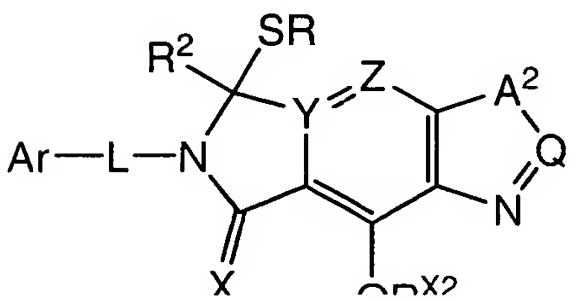












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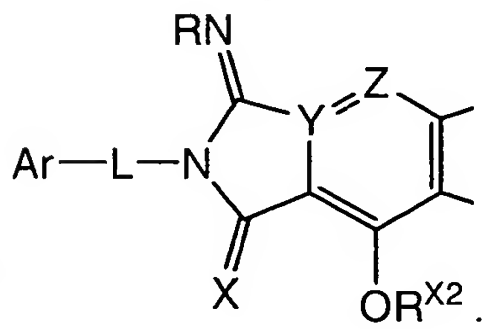

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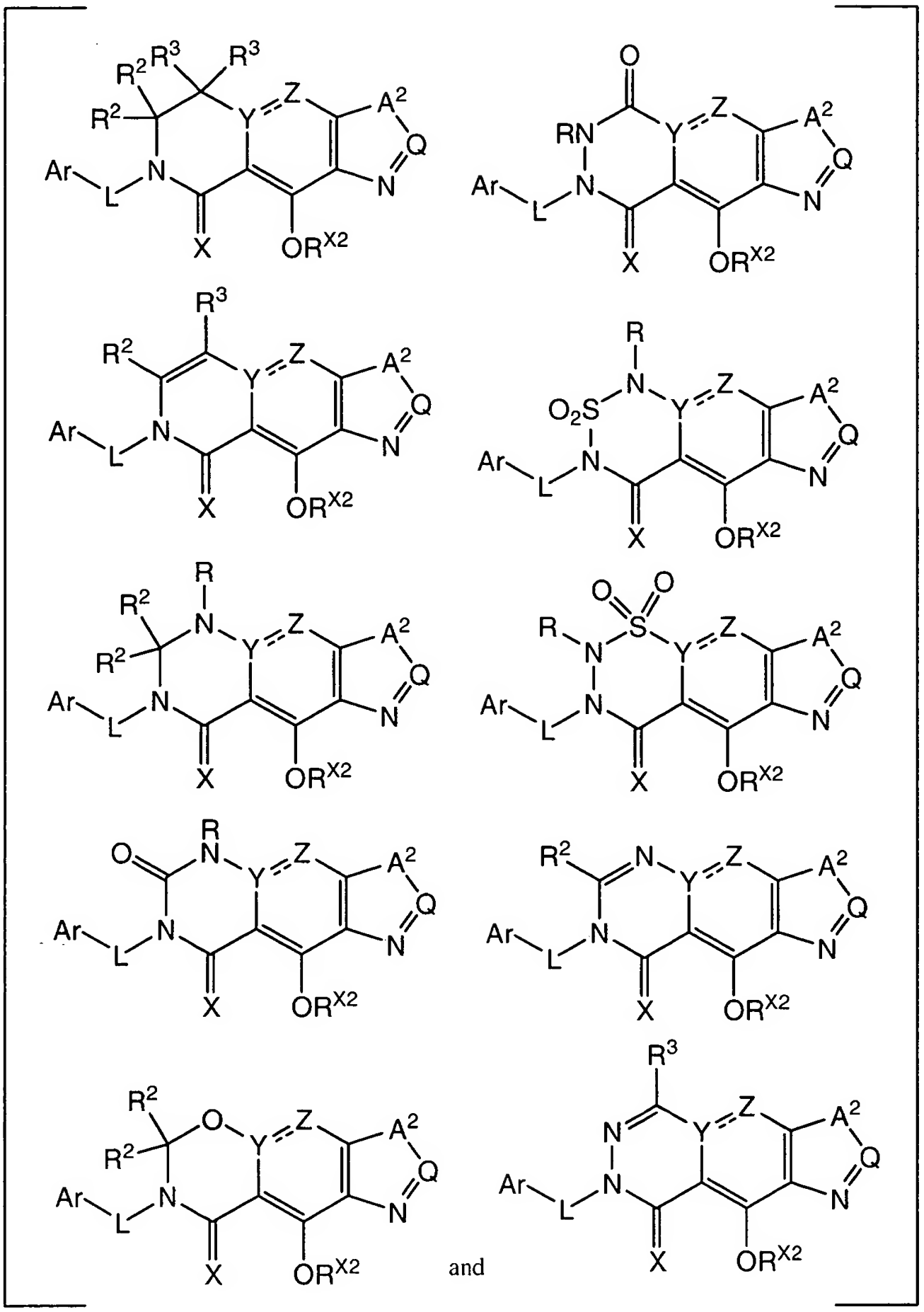
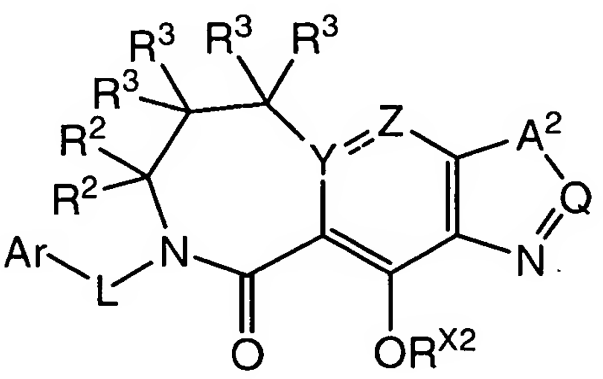
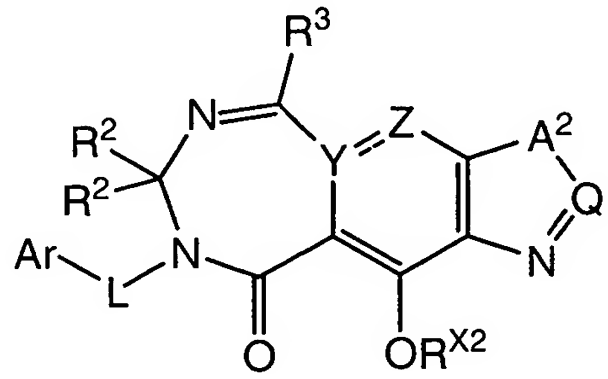
3. (Currently amended): A compound of claim 1 [selected from the structures:] wherein A^1 is CH_2.

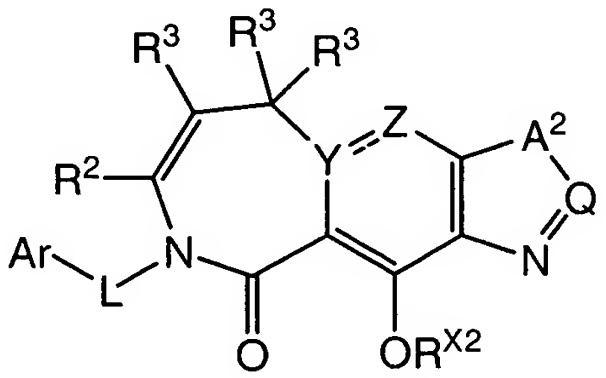


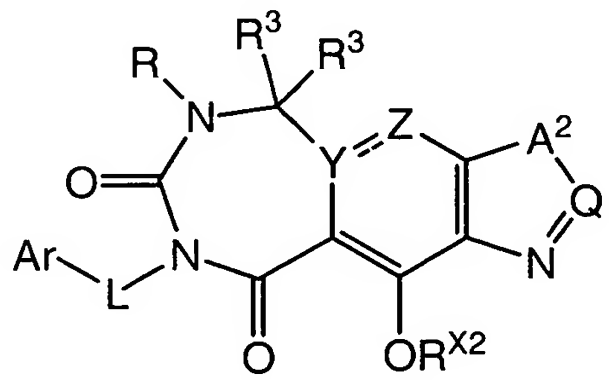
and

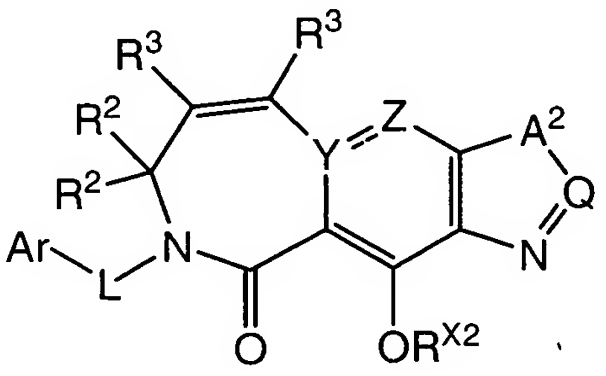
4. (Currently amended): A compound of claim 1 [selected from the structures:] wherein Ar is a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms.

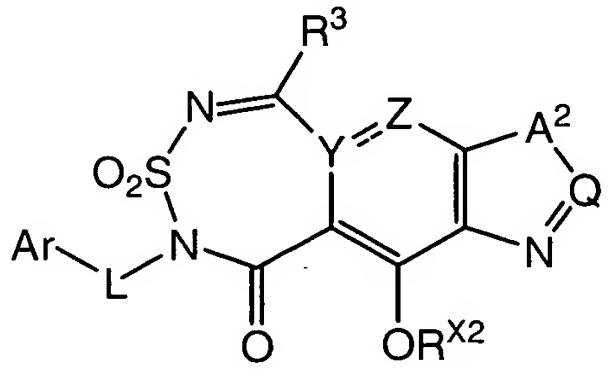












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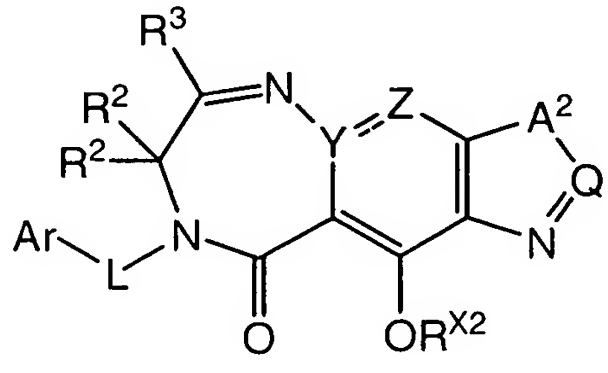
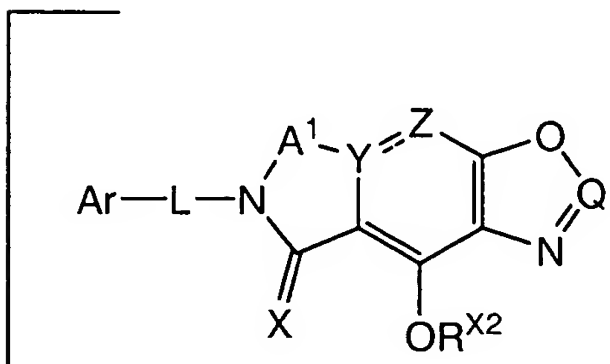
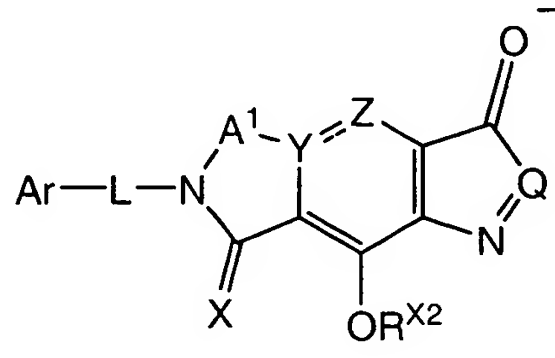
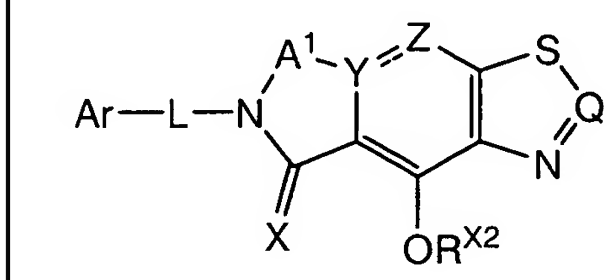
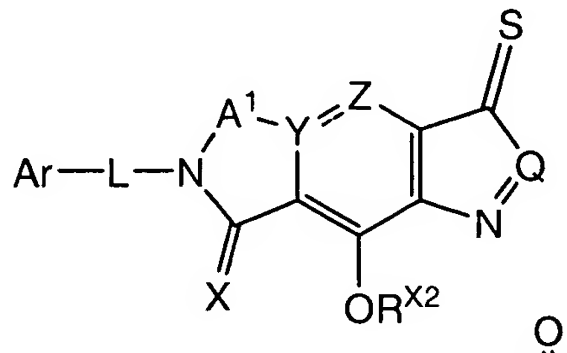


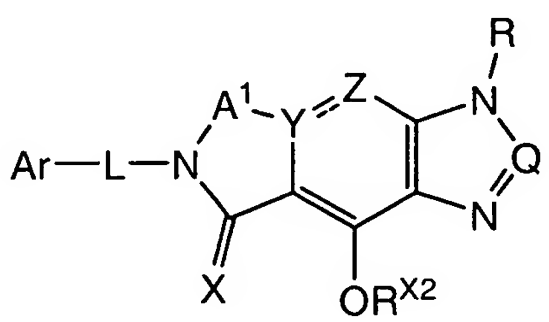
5. (Currently amended): A compound of claim 1 [selected from the structures:] wherein R^1 is selected from R, OR, NR_2, NHR, $NHSO_2R$ and $NRSO_2R$;

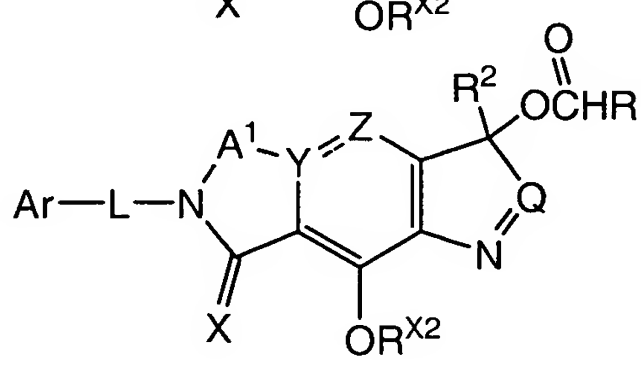


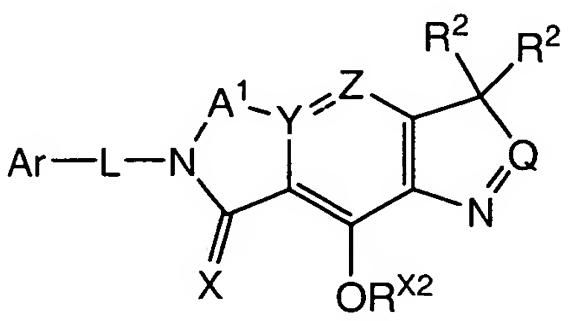


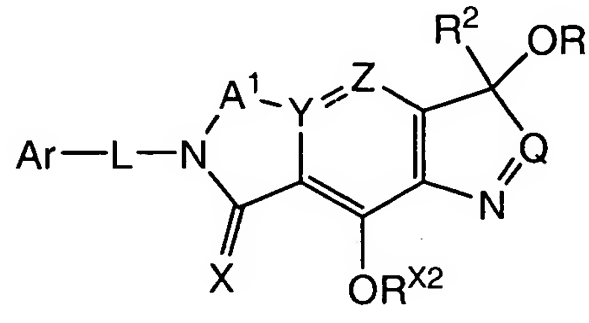


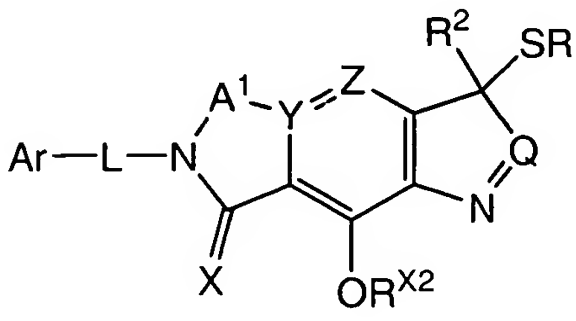












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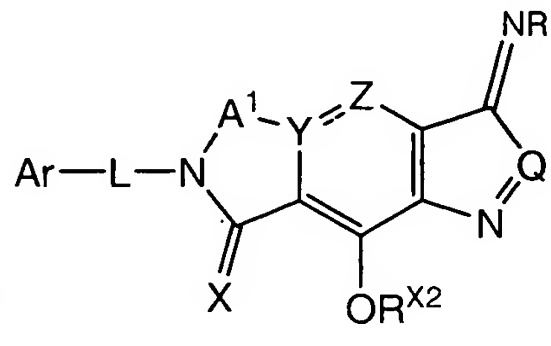
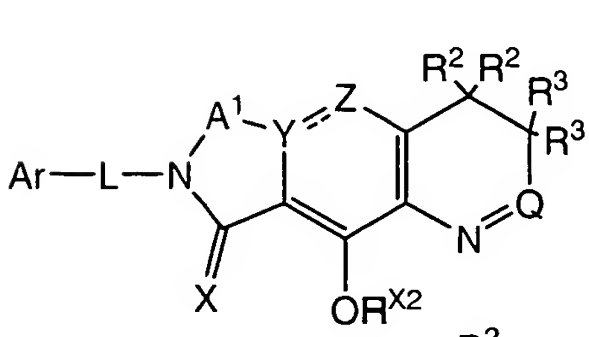
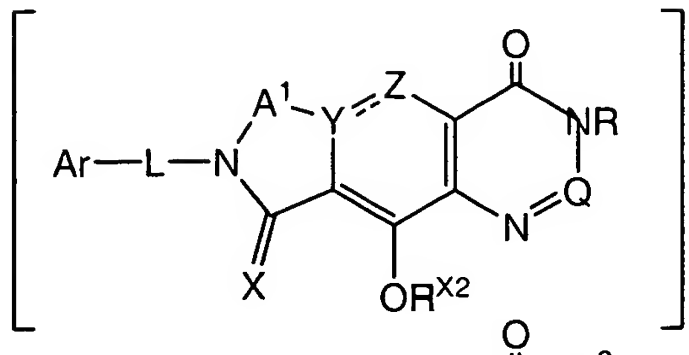
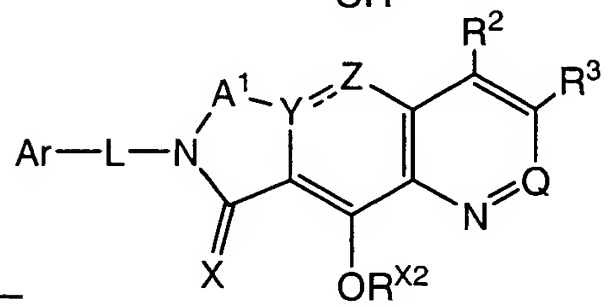
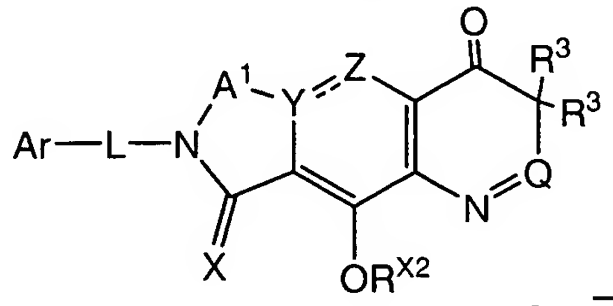


6. (Currently amended): A compound of claim 1 selected from the structures:









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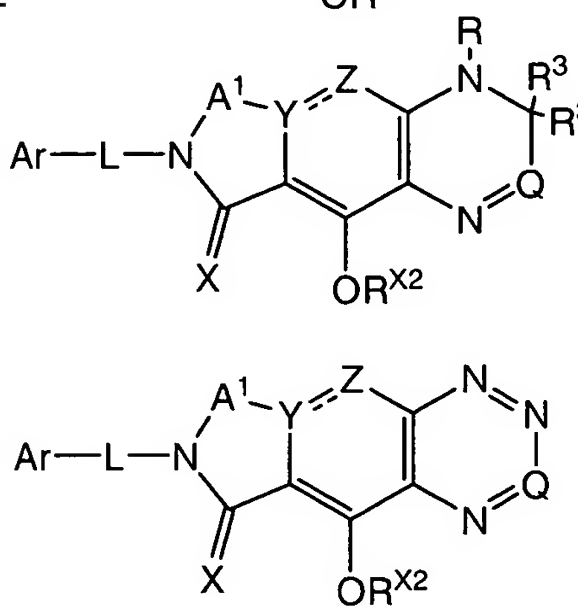

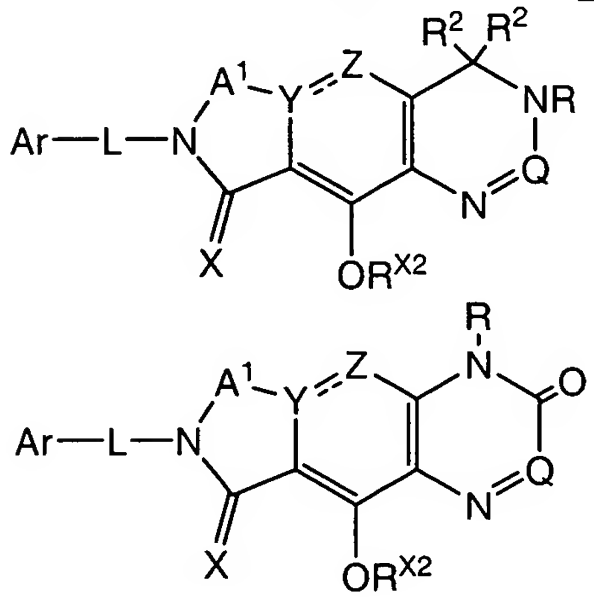

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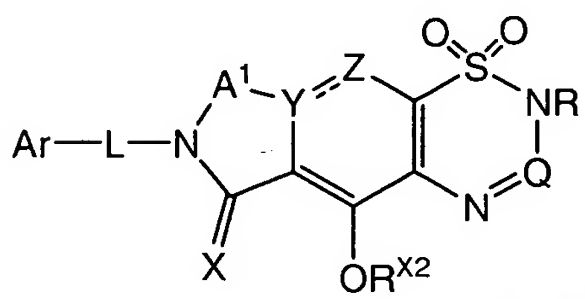
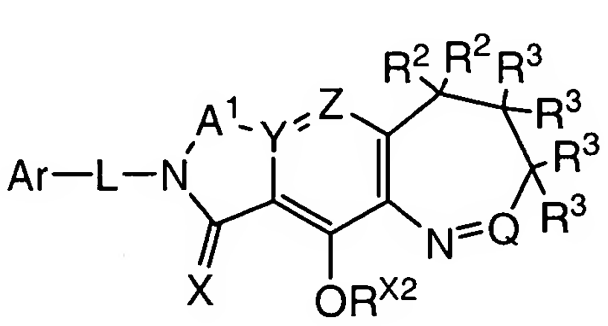
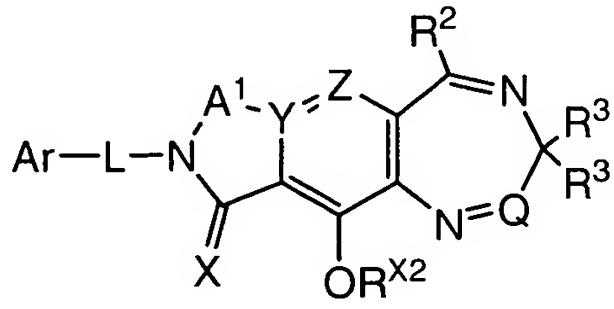
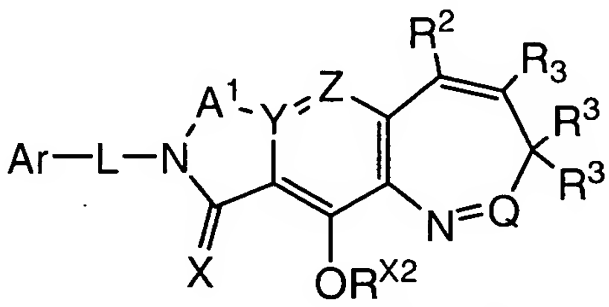
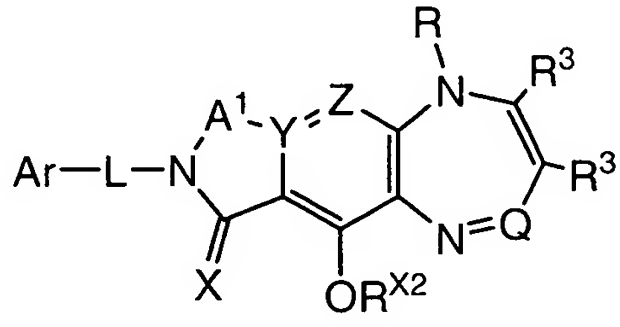


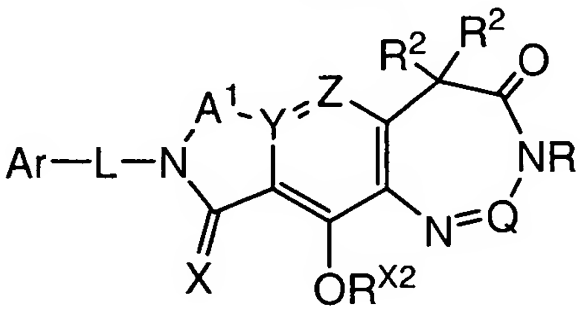
7. (Currently amended): A compound of claim 1 [selected from the structures:] wherein R^{x2} is a protecting group selected from the group consisting of benzyhydryl ($CHPh_2$), trialkylsilyl (R_3Si), 2-trimethylsiloxyethyl, alkoxymethyl (CH_2OR), and ester (C(=O)R).

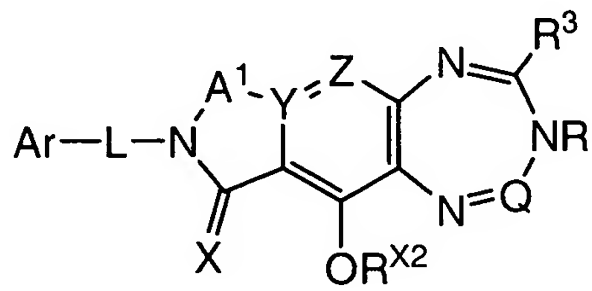




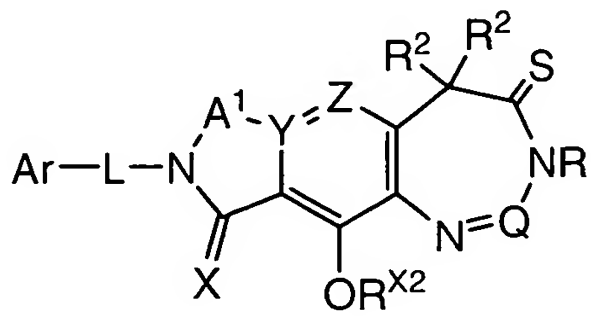




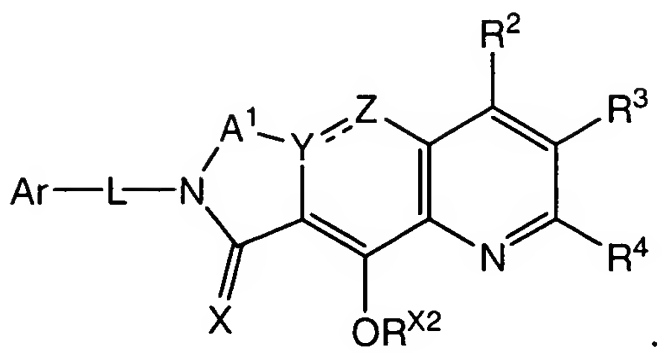




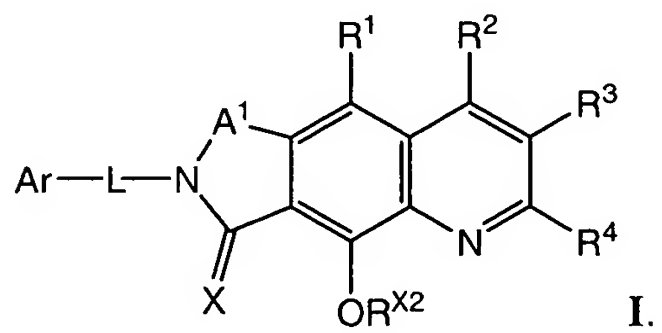
and



8. (Currently amended): A compound of claim [6] 1 having the structure:



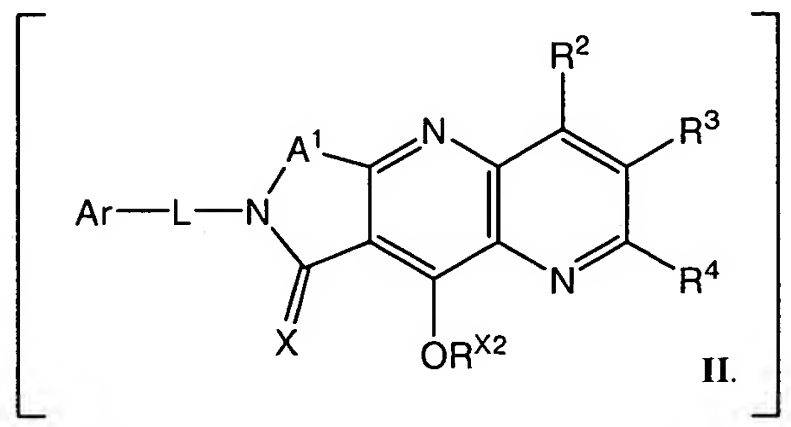
9. (Currently amended): A compound of claim [6] 1 having Formula I:



I.

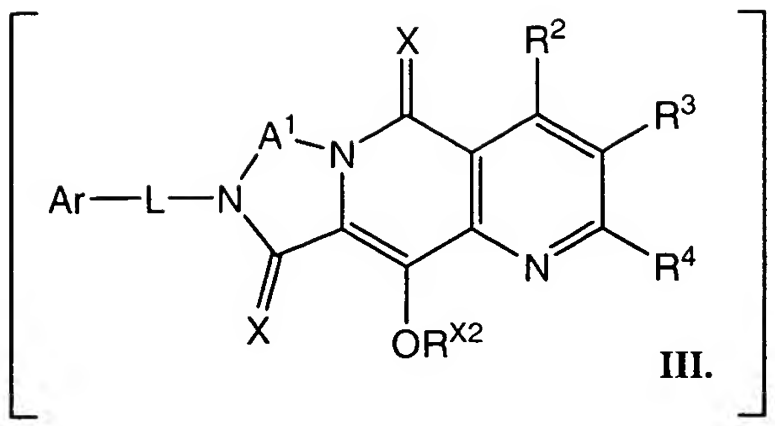
wherein R^{x2} is H and X is O.

10. (Currently amended): A compound of claim [6 having Formula II:] 1 wherein L is not a bond.



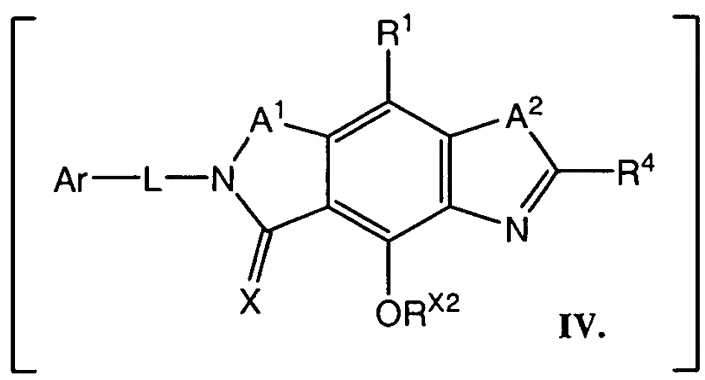
II.

11. (Currently amended): A compound of claim [6 having Formula III:] 1 wherein R^4 is H.



III.

12. (Currently amended): A compound of claim 1 [having Formula IV:] wherein Ar is $C_6 - C_{20}$ substituted aryl.

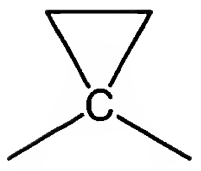


IV.

13. (Currently amended): A compound of claim 1 having [comprising] at least one phosphonate group.

14. (previously presented): A compound of claim 1 wherein substituted alkyl, substituted alkylene, substituted alkyenylene, substituted alkynylene, substituted carbocycle, substituted aryl, and substituted heteroaryl are independently substituted with one or more substituents selected from F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, $-NHR$, $-NR_2$, $-NR_3^+$, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1-C_8 alkoxy, C_1-C_8 trifluoroalkyl, C_1-C_8 alkyl, C_3-C_{12} carbocycle, C_6-C_{20} aryl, C_2-C_{20} heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

15. (previously presented): The compound of claim 1 wherein A^1 is CH_2, $C(CH_3)_2$,



, CH_2–CH_2, $C(CH_3)_2$–CH_2, or CH_2–CH_2–CH_2 .

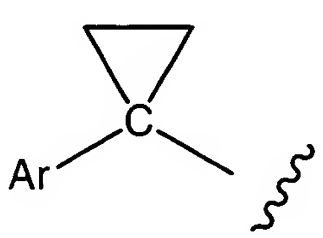
16. (previously presented): The compound of claim 9 wherein X is O; L is CH_2; and Ar is substituted phenyl.

17. (previously presented): The compound of claim 16 wherein Ar is 4-fluorophenyl.

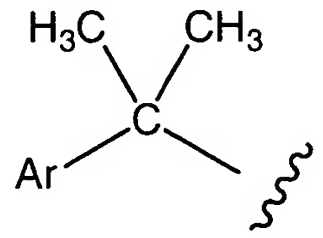
18. (previously presented): The compound of claim 9 wherein X is O; and R^2, R^3 and R^4 are each H.

19. (previously presented): The compound of claim 9 wherein X is O; A^1 is CH_2; and R^2, R^3 and R^4 are each H.

20. (previously presented): The compound of claim 1 wherein Ar-L is selected from the structures:

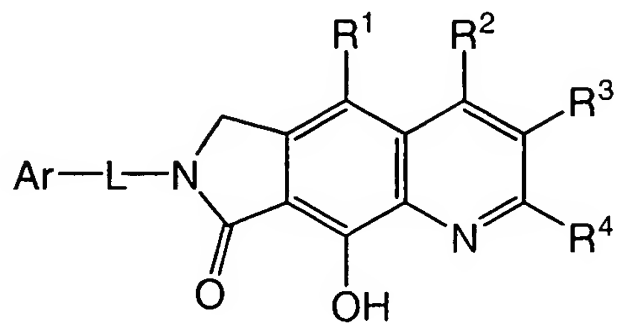


and

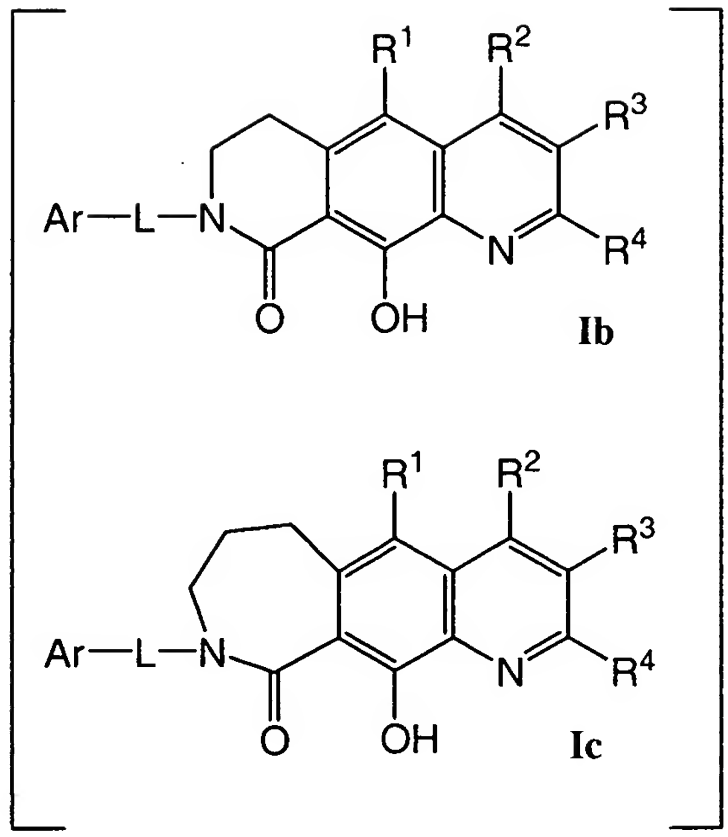


.

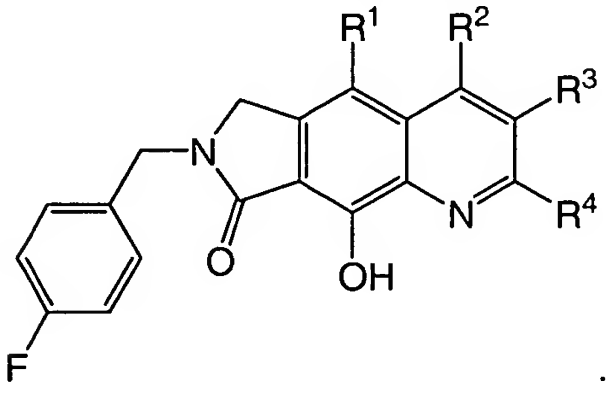
21. (Currently amended): A compound of claim 9 <u>having</u> [comprising] Formula Ia[, Ib, or Ic]:



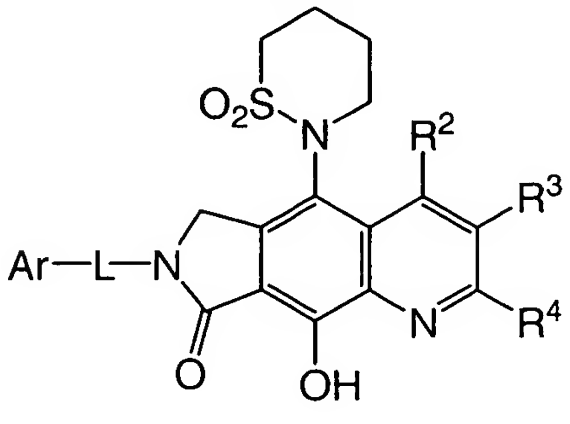
Ia



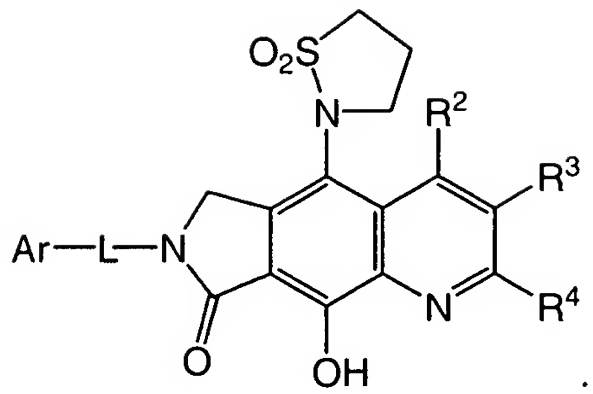
22. (previously presented): A compound of claim 9 having the structure:



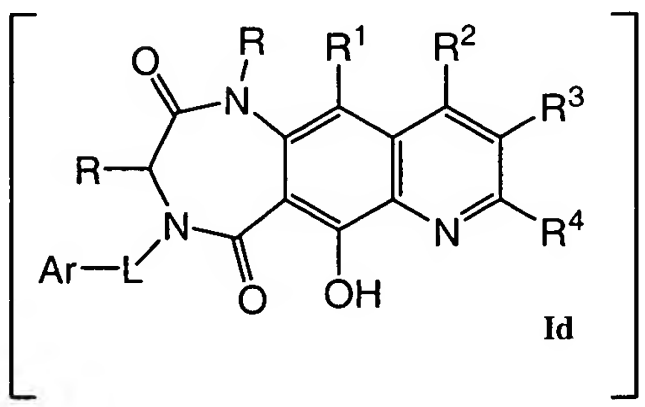
23. (previously presented): A compound of claim 22 selected from the structures:



and

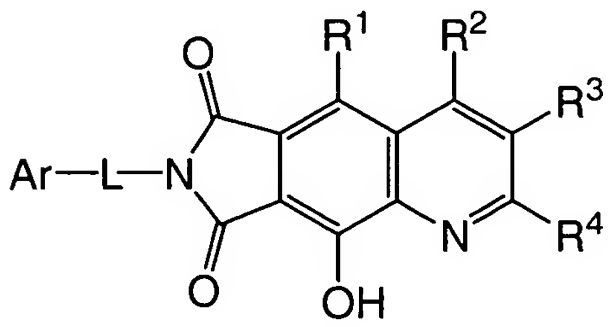


24. (Currently amended): A compound of claim 9 [having Formula Id:] wherein AR-L is para-fluorobenzyl.



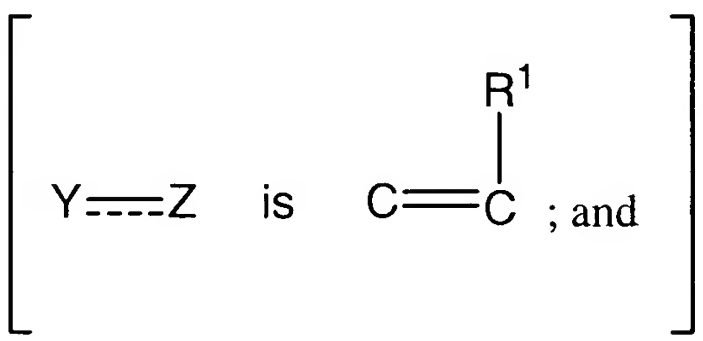
Id

25. (previously presented): A compound of claim 9 having the structure:



with the proviso that when R^1 is OH, and R^2, R^3, and R^4 are H, then L is not a bond.

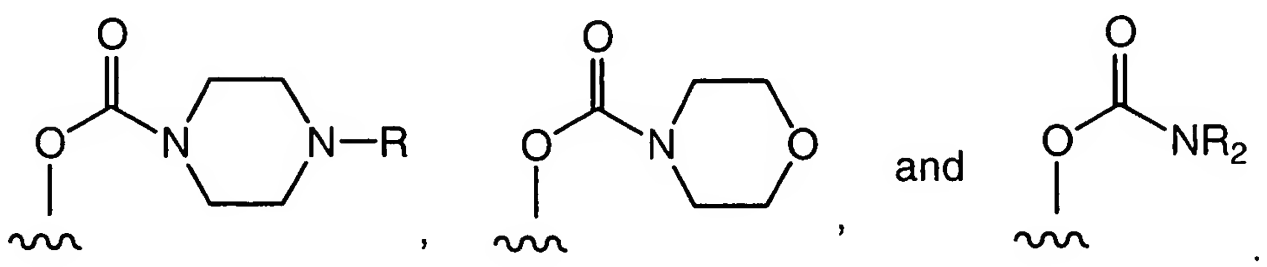
26. (Currently amended): A compound of claim 1 wherein



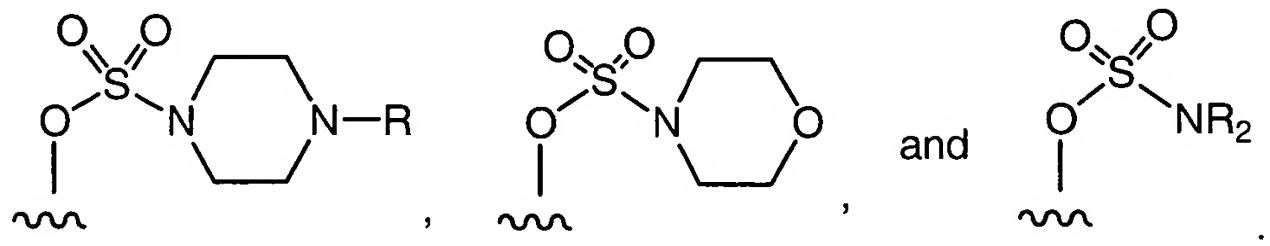
R^1 is selected from CR_3, $C(=O)NR_2$, $OC(=O)OR$, $OC(=O)NR_2$, $OC(=O)R$, OSO_2NR_2 (sulfamate), NR_2, $NRSO_2R$, SR, S(O)R, SO_2R and [or] SO_2NR_2 (sulfonamide).

27. (previously presented): The compound of claim 26 wherein at least one R is [comprises] a prodrug moiety.

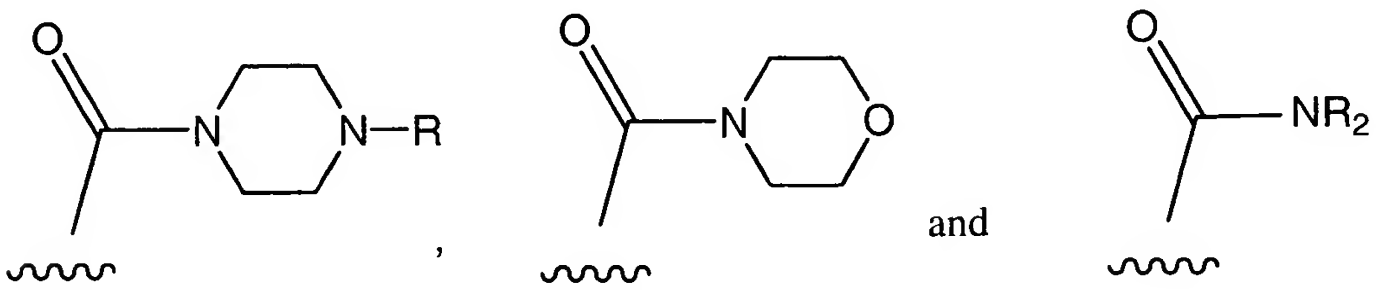
28. (previously presented): A compound of claim 1 wherein at least one of R^1, R^2, R^3, and R^4 is selected from the structures:



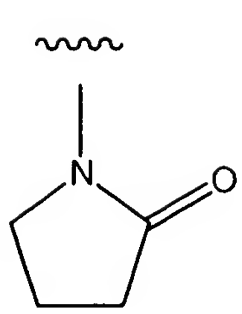
29. (previously presented): A compound of claim 1 wherein at least one of R^1, R^2, R^3, and R^4 is selected from the structures:

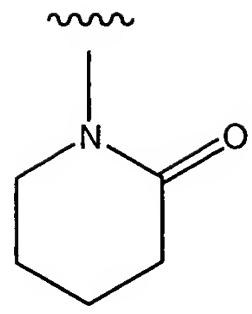


30. (previously presented): A compound of claim 1 wherein at least one of R^1, R^2, R^3, and R^4 is selected from the structures:



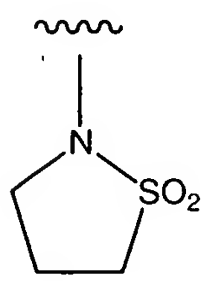
31. (previously presented): A compound of claim 1 wherein at least one of R^1, R^2, R^3, and R^4 [comprise] is a lactam having the structures:

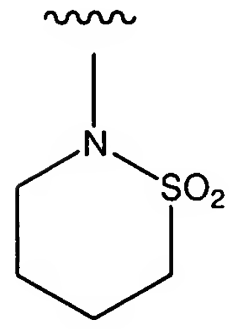


and


, or

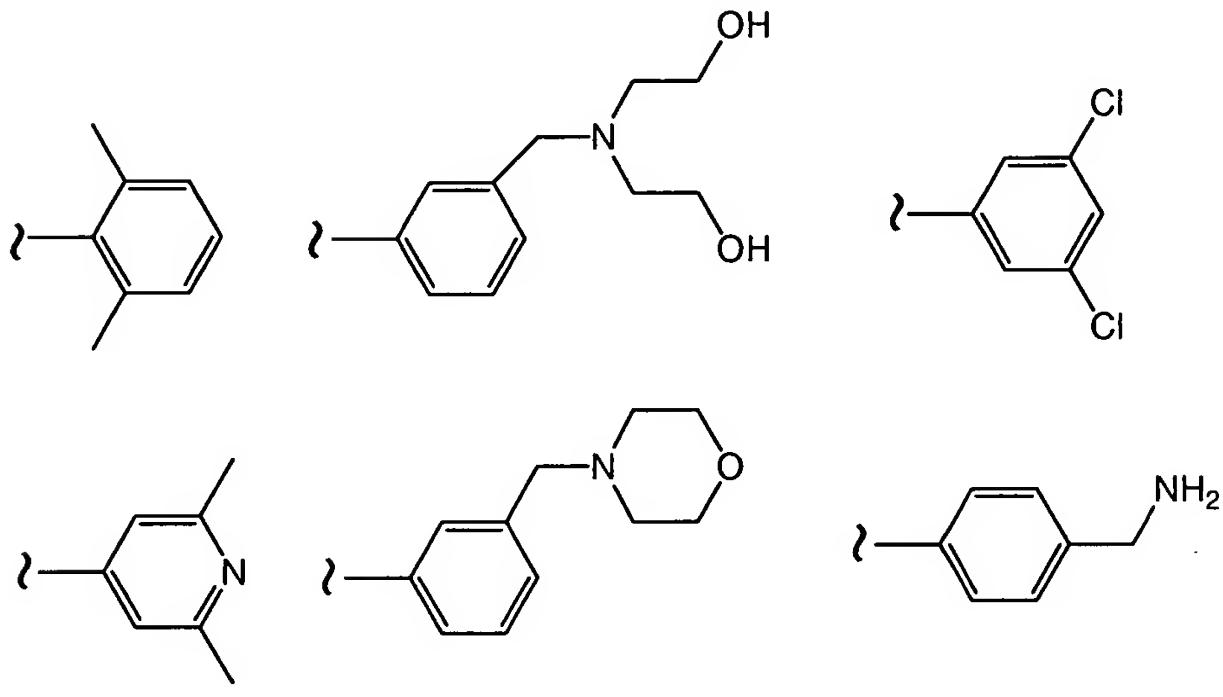
a sultam having the structures:

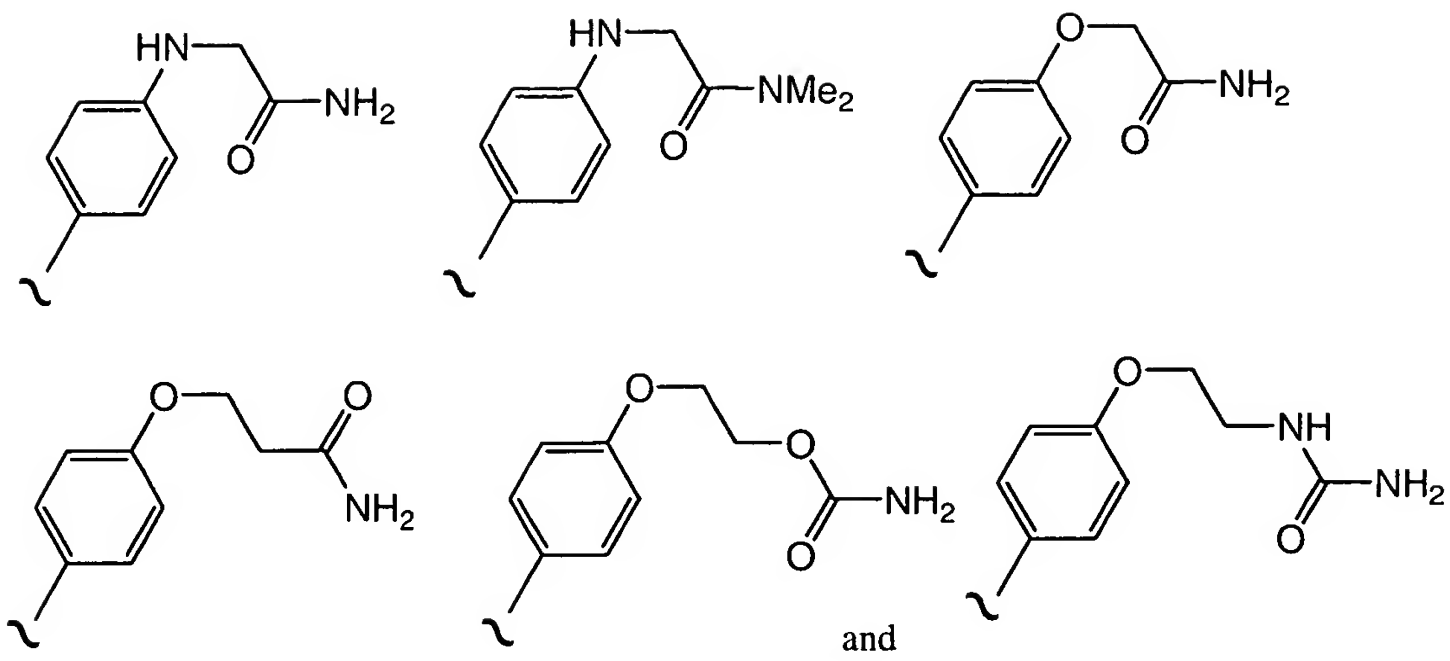


and


.

32. (previously presented): A compound of claim 1 wherein Ar is selected from the structures:

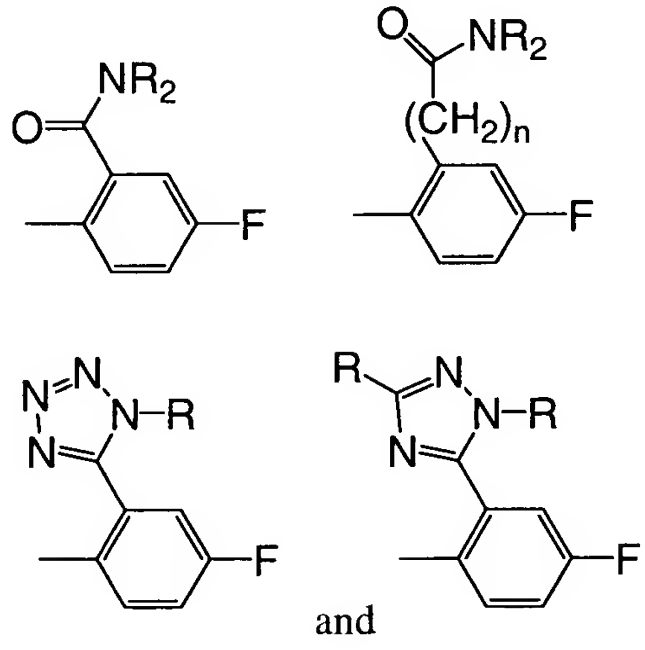




and

where the wavy line ~ indicates the covalent attachment site to L.

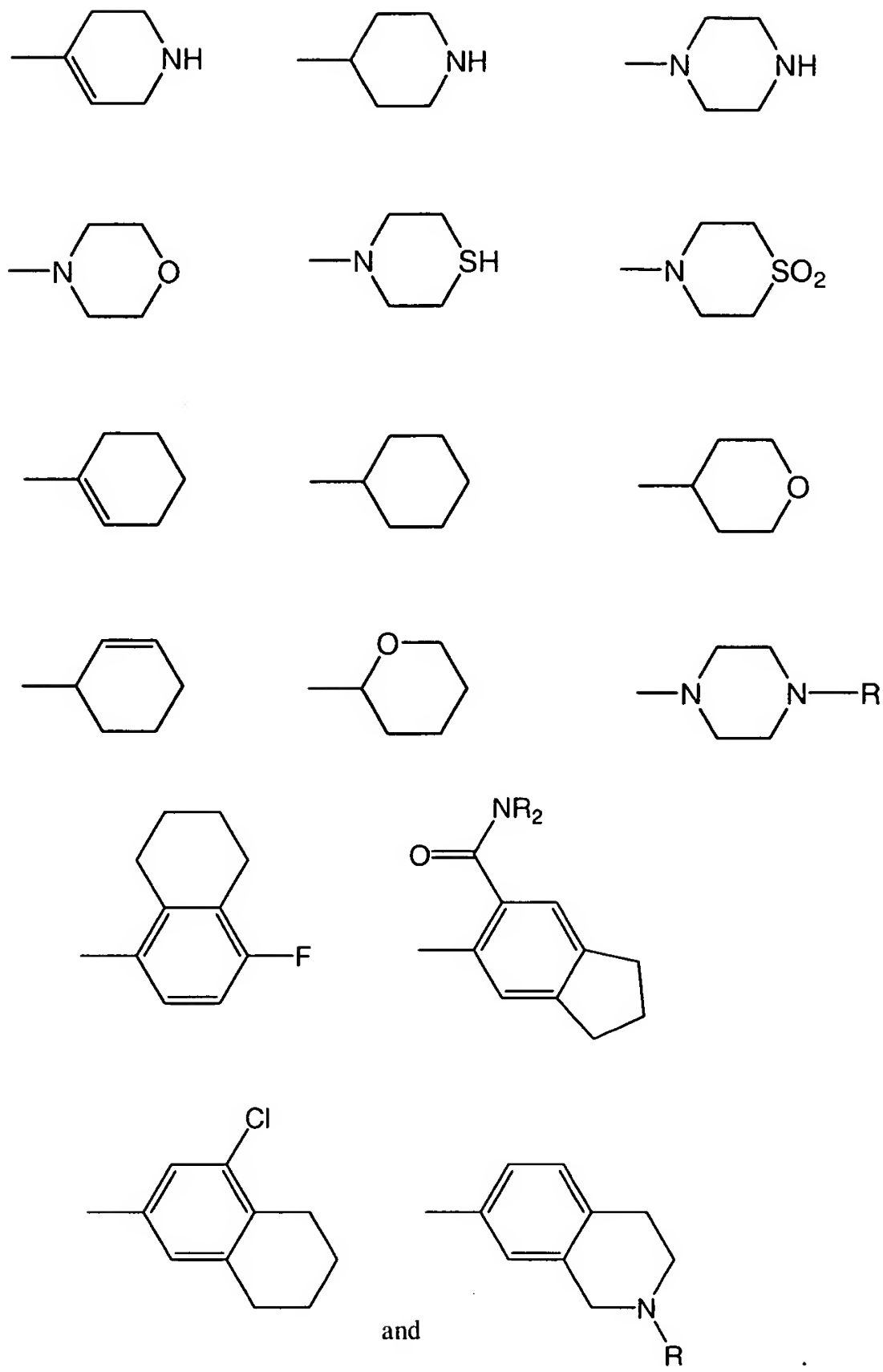
33. (previously presented): A compound of claim 1 wherein Ar is selected from the structures:



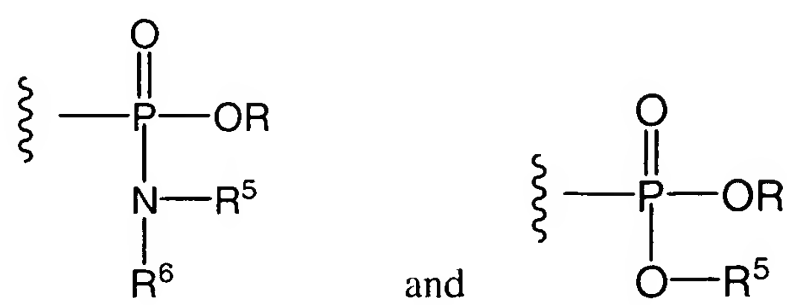
and

where n is 1 to 6.

34. (previously presented): A compound of claim 1 wherein Ar is selected from the structures:

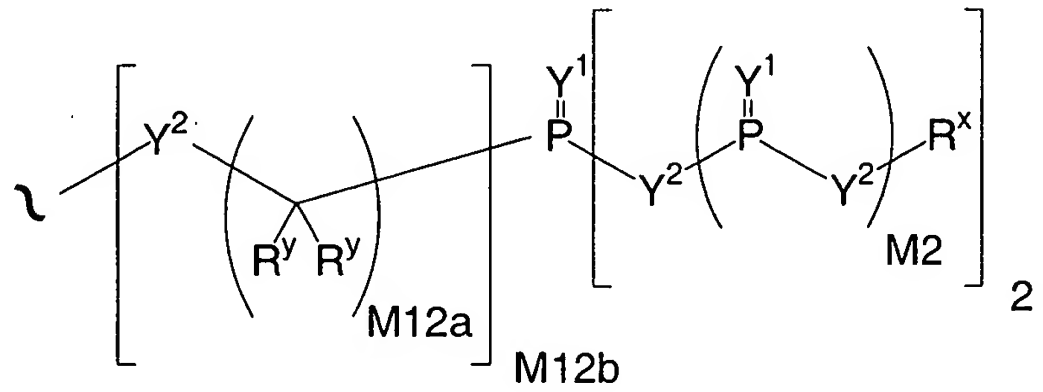


35. (previously presented): A compound of claim 1 comprising a prodrug moiety selected from the structures:



wherein R^5 is $-CR_2CO_2R^7$ where R^6 and R^7 are independently H or C_1–C_8 alkyl.

36. (previously presented): The compound of claim 1 comprising a phosphonate or prodrug moiety having the structure:



wherein:

Y^1 is independently O, S, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, or $N(N(R^x)_2$;

Y^2 is independently a bond, O, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, $N(N(R^x)_2)$, -S(O)- (sulfoxide), $-S(O)_2-$ (sulfone), -S- (sulfide), or -S-S- (disulfide);

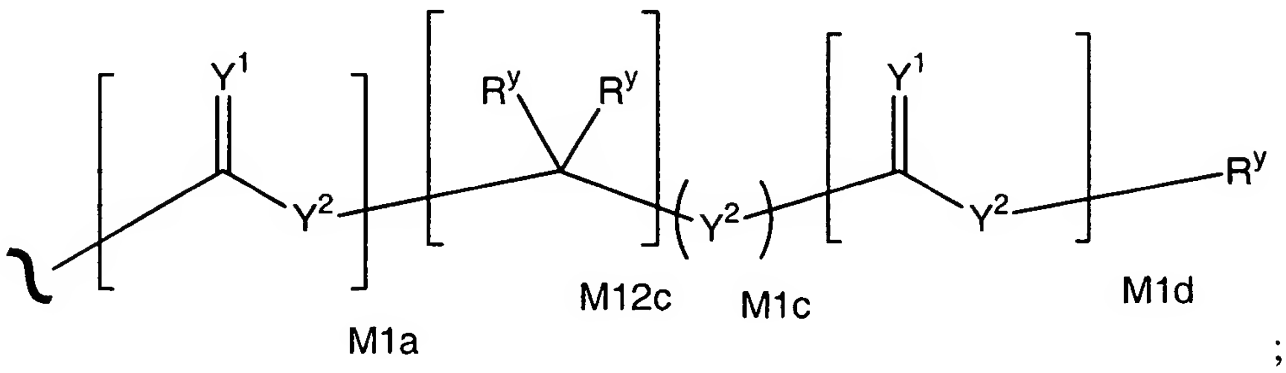
M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

R^y is independently H, C_1–C_6 alkyl, C_1–C_6 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, or a protecting group, or where taken together at a carbon atom, two vicinal R^y groups form a carbocycle or a heterocycle; and

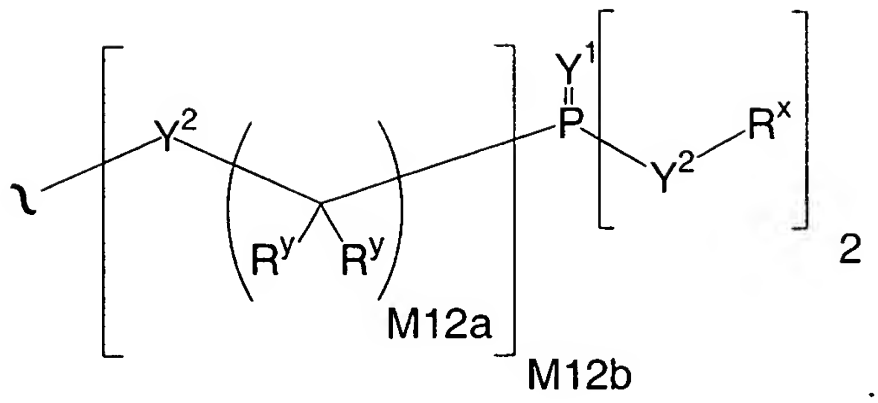
R^x is independently H, C_1–C_6 alkyl, C_1–C_6 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, or a protecting group, or the formula:



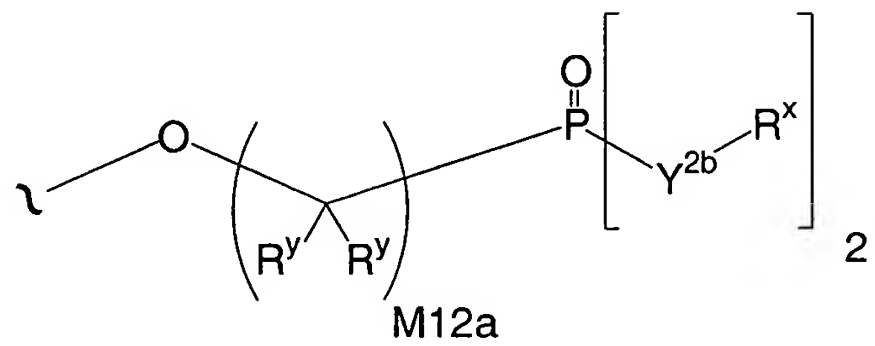
;

where M1a, M1c, and M1d are independently 0 or 1, and M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

37. (previously presented): The compound of claim 36 wherein the phosphonate or prodrug moiety has the structure:

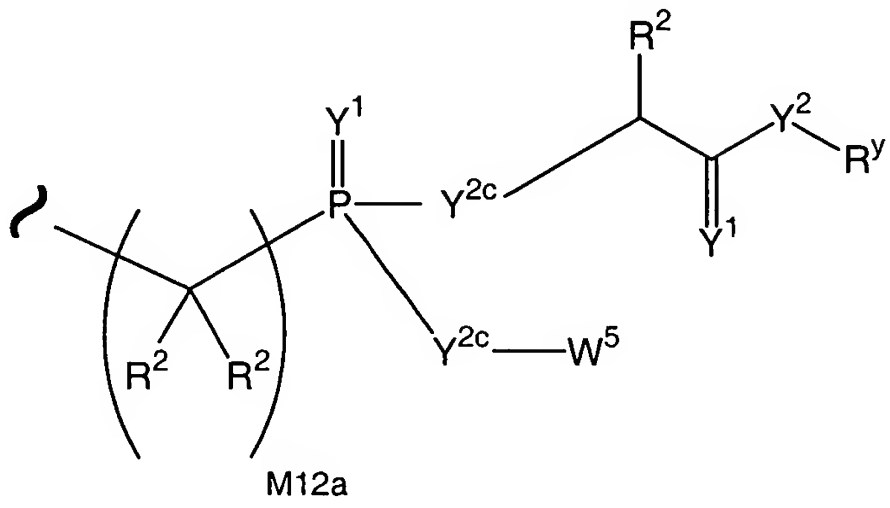


38. (previously presented): The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:



where Y^{2b} is O or $N(R^x)$.

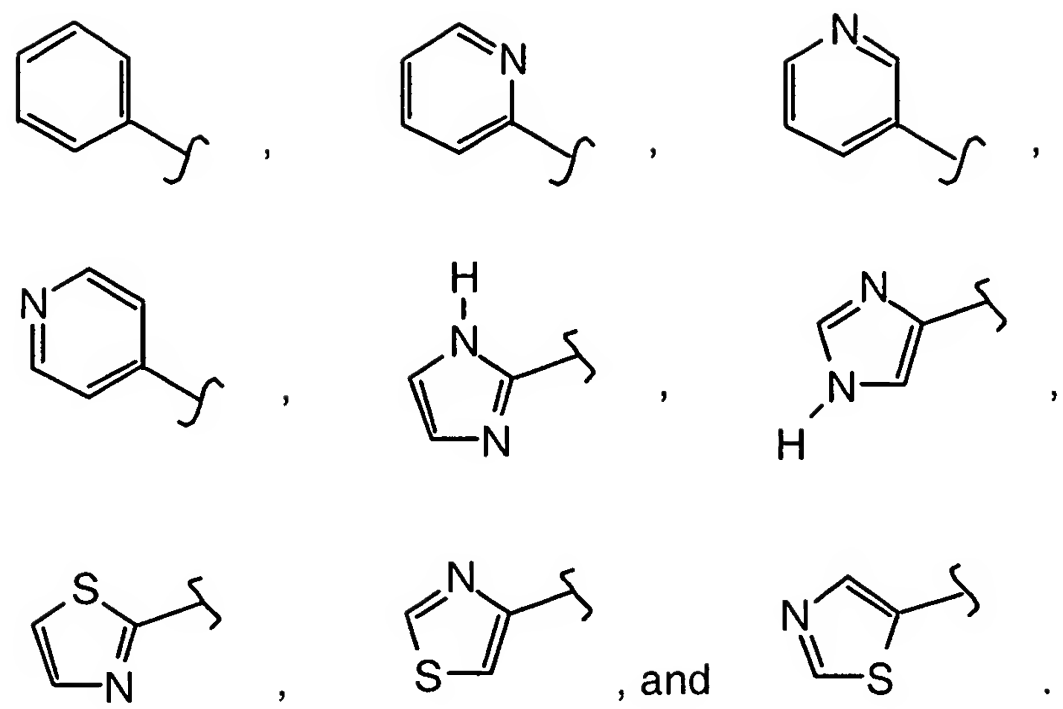
39. (previously presented): The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:



;

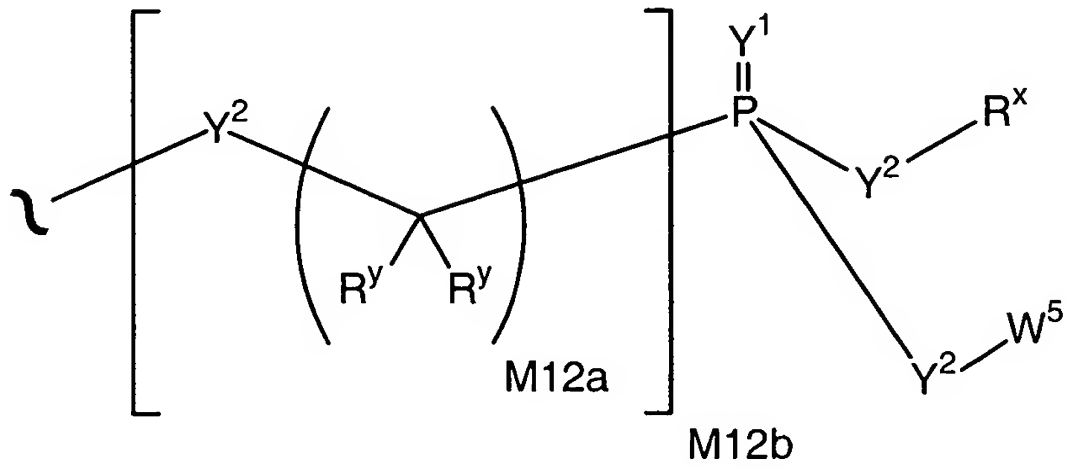
where W^5 is a carbocycle, and Y^{2c} is O, $N(R^y)$ or S.

40. (previously presented): The compound of claim 39 wherein W^5 is selected from the structures:



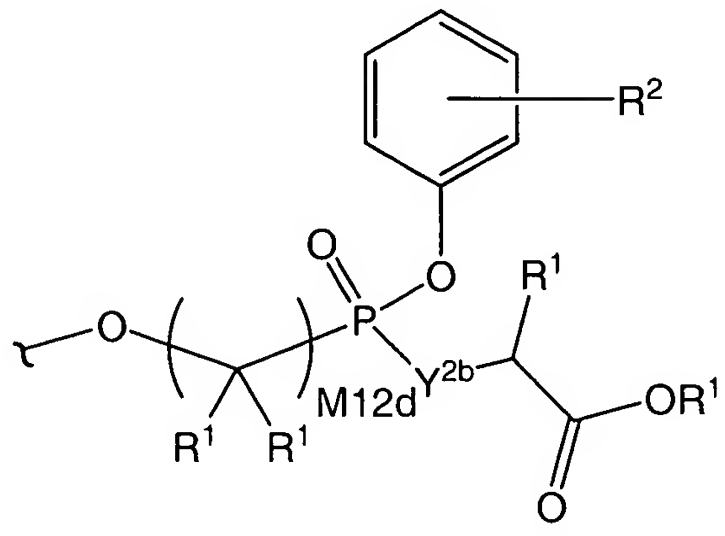
, and .

41. (previously presented): The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:



.

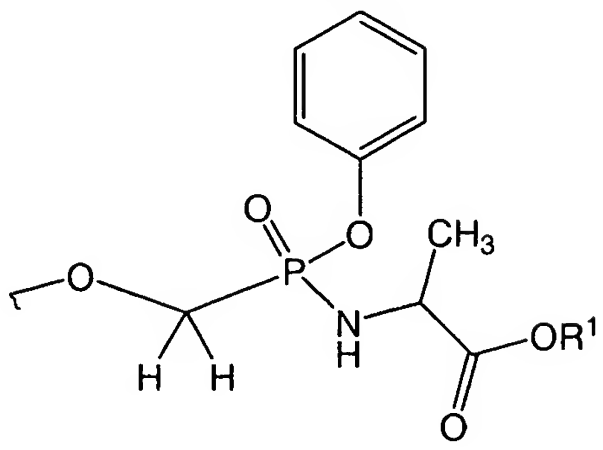
42. (Currently amended): The compound of claim 1 [41] wherein the phosphonate or prodrug moiety has the structure:



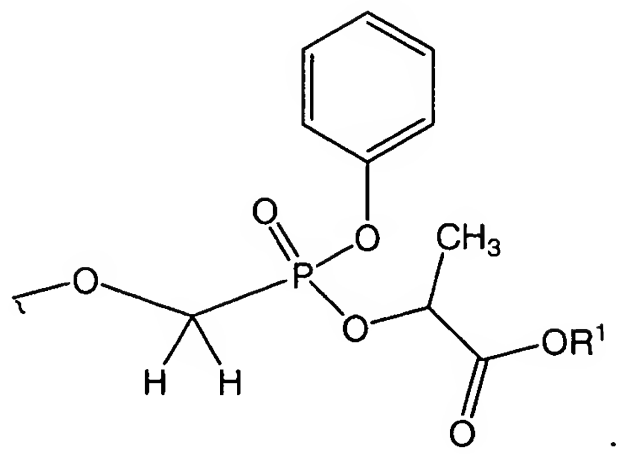
wherein Y^{2b} is O or N(R^x); M12d is 1, 2, 3, 4, 5, 6, 7 or 8; R^1 is H or C_1–C_6 alkyl; and the phenyl carbocycle is substituted with 0 to 3 R^2 groups where R^2 is C_1–C_6 alkyl or substituted

alkyl.

43. (Currently amended): The compound of claim 1 [42] wherein the phosphonate or prodrug moiety has the structure:

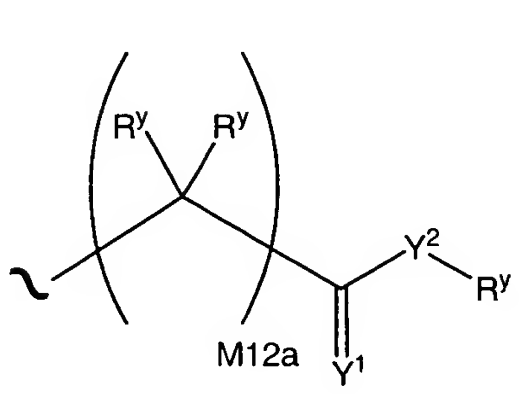


or

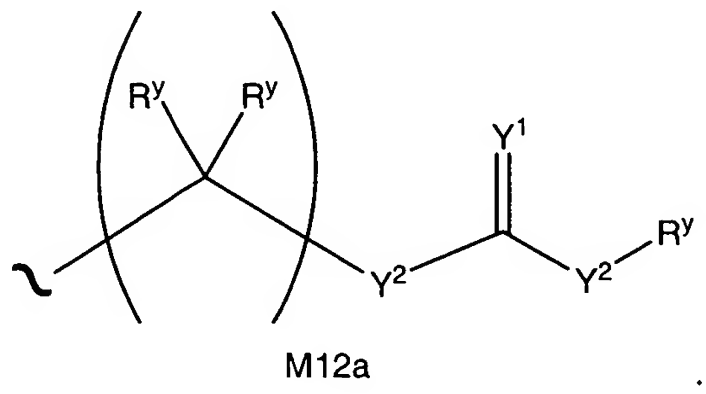


.

44. (previously presented): The compound of claim 36 wherein R^x is selected from the structures:

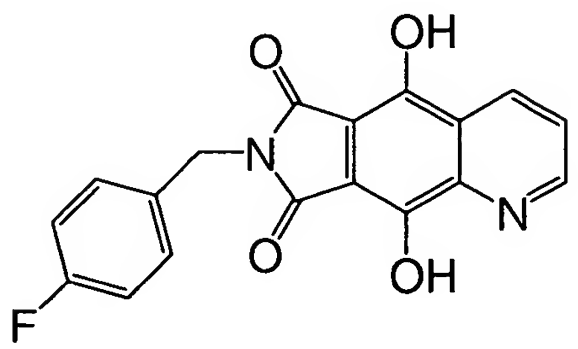


and



.

45. (Currently amended): A compound of [claim 9] selected from the structures:



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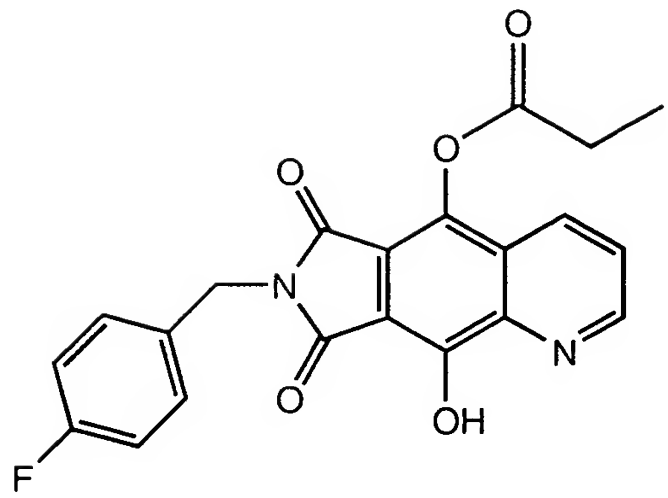

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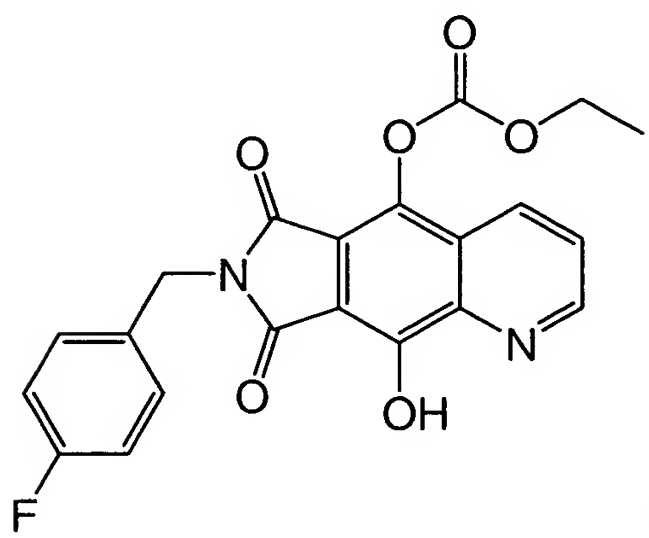

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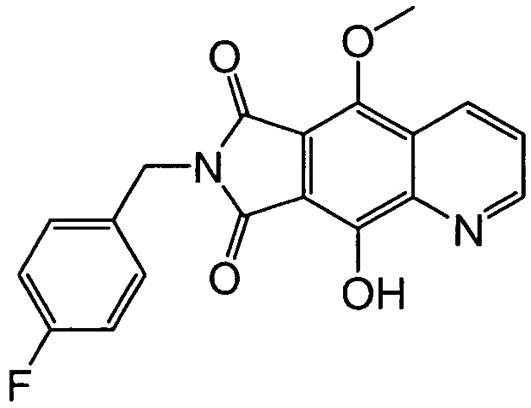

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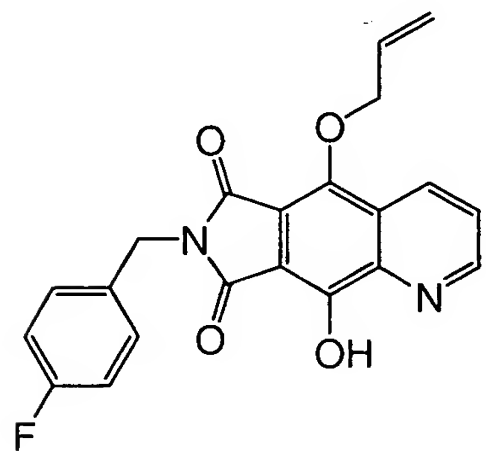

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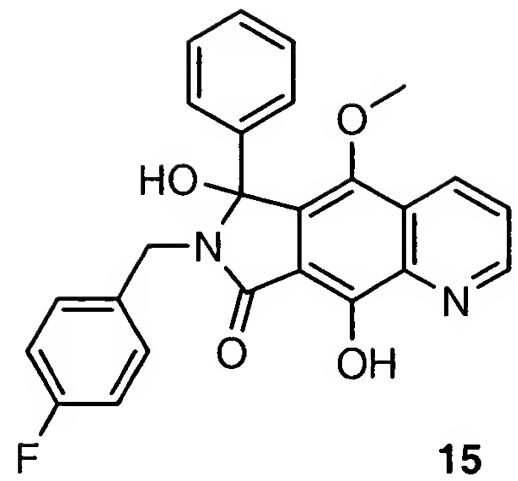

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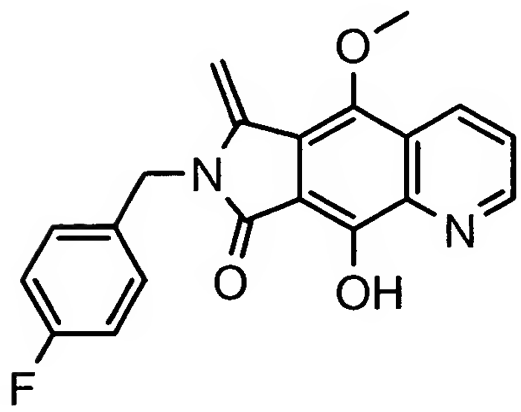

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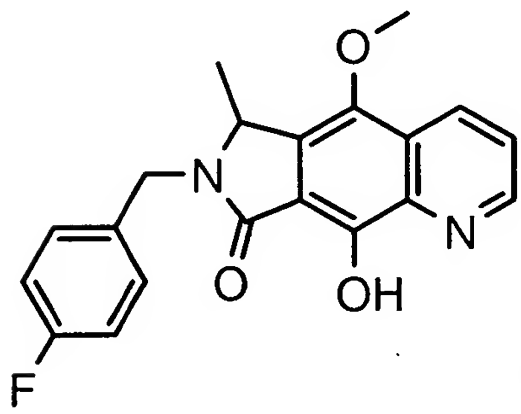

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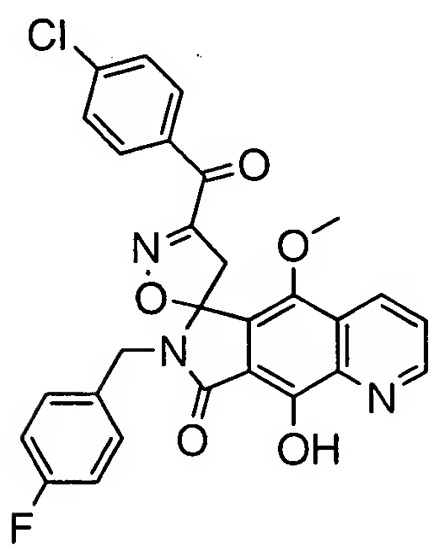

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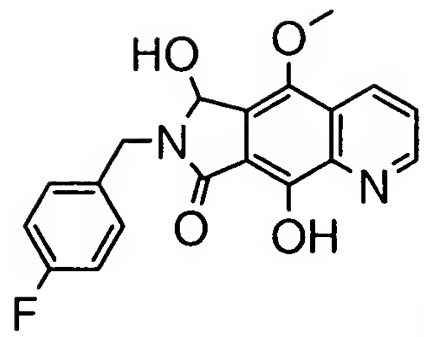

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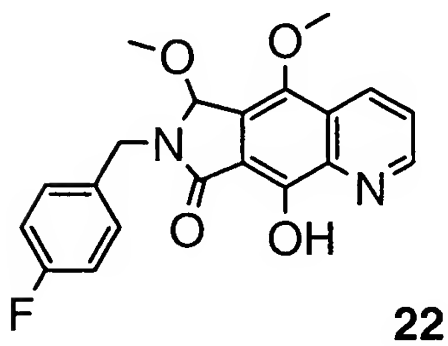

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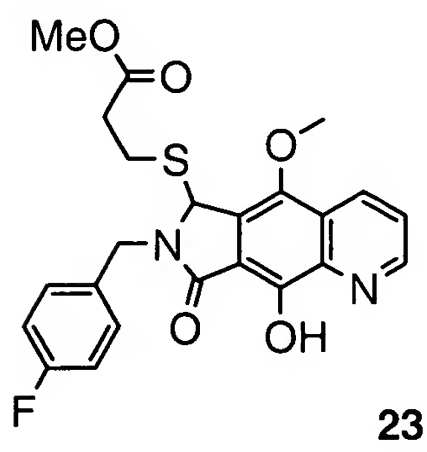

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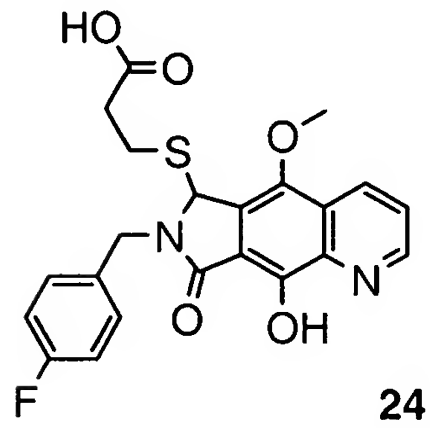
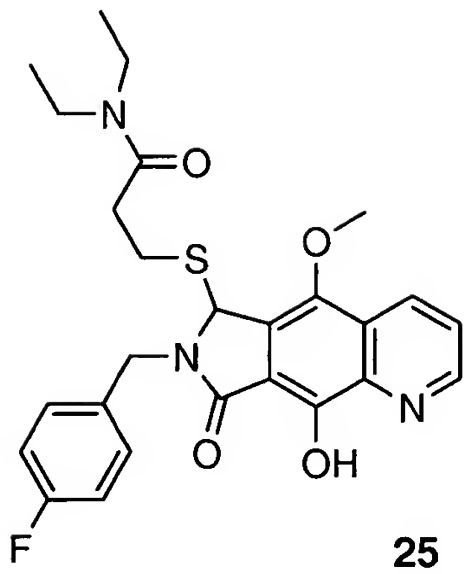


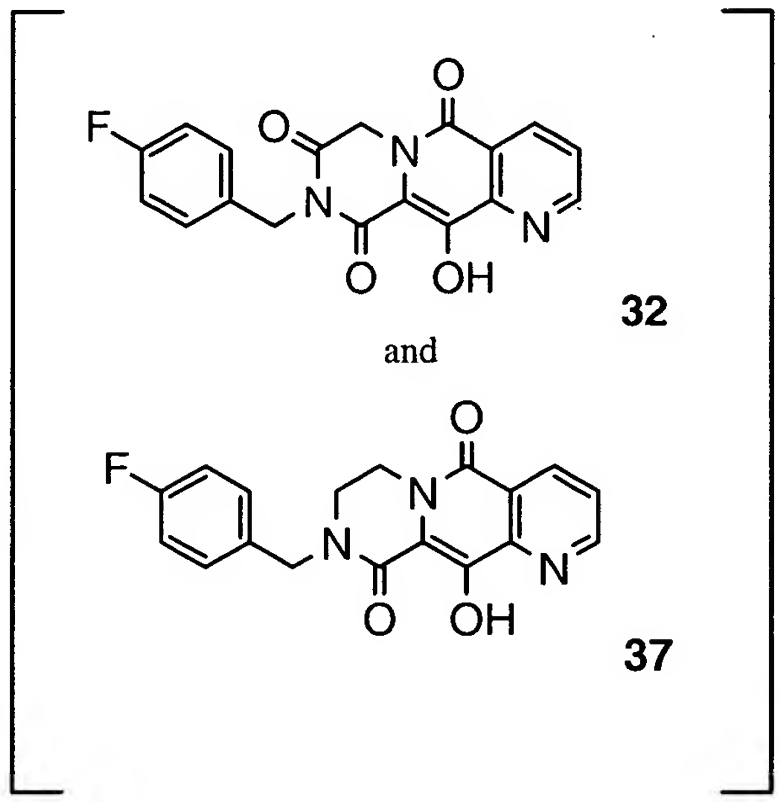
24

and

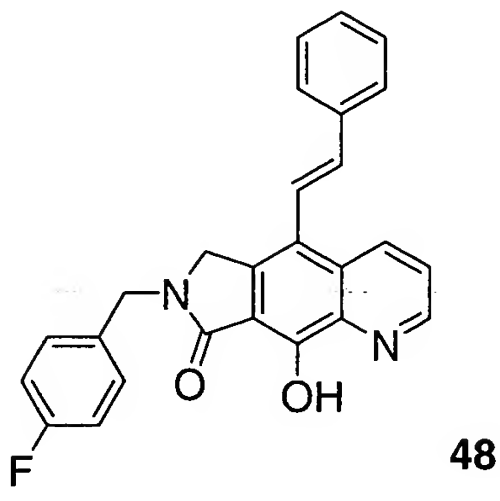


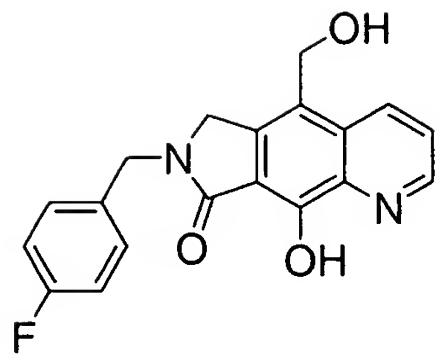
25

46. (Currently amended): A compound of claim 1 [11 selected from the structures:] wherein none of R^2, R^3, R^4, R, or R^{x2} is a prodrug moiety



47. (Currently amended): A compound of [claim 9] selected from the structures:





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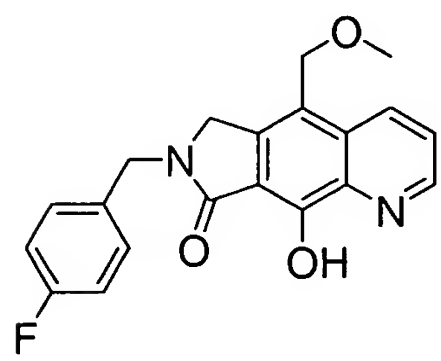

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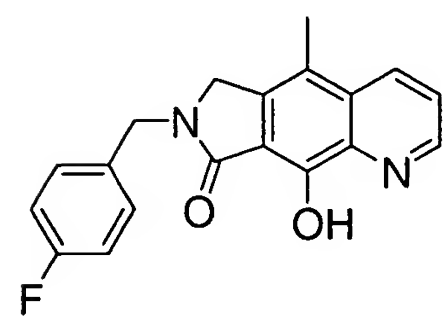

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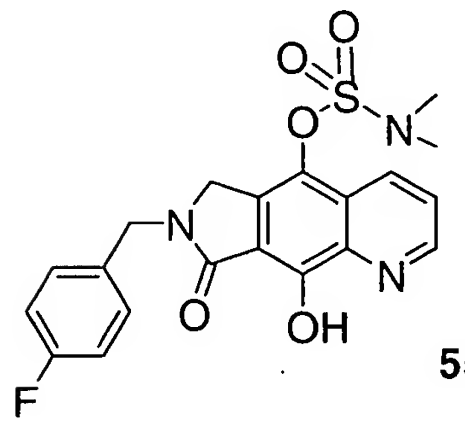

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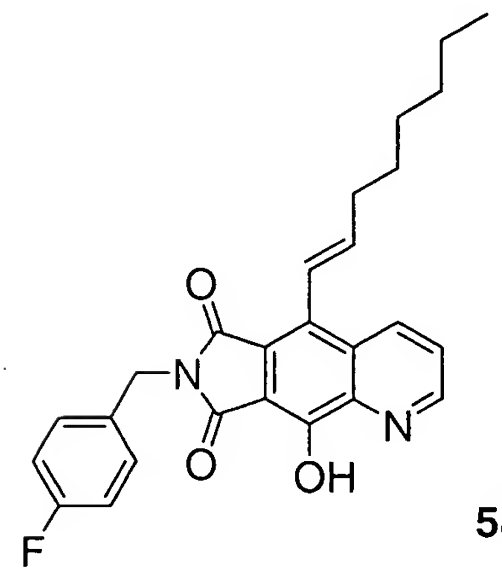

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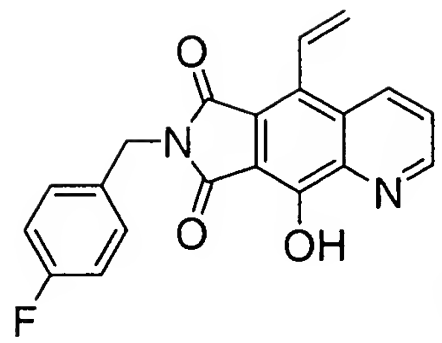

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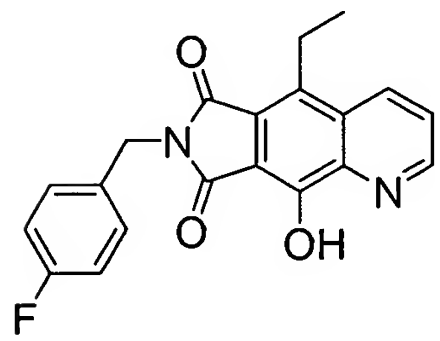

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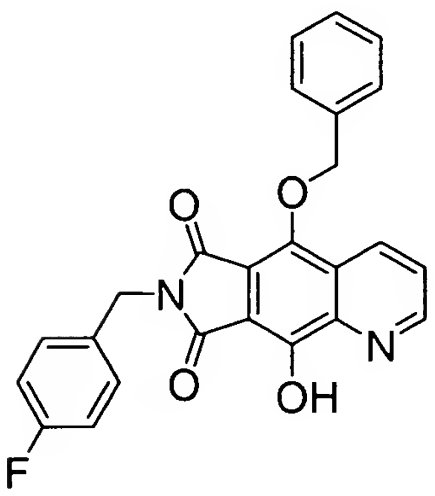

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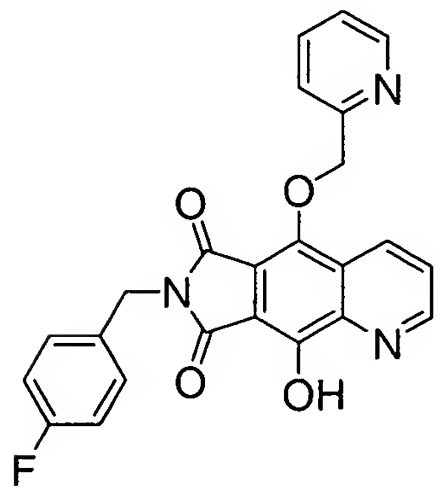

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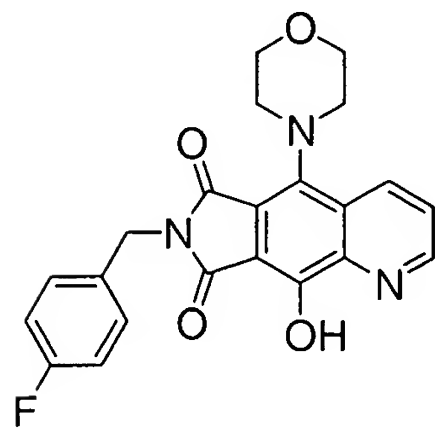

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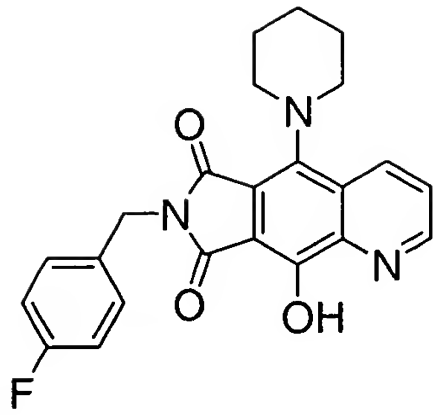

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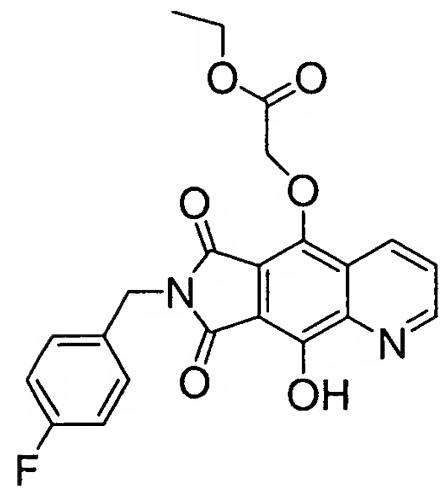

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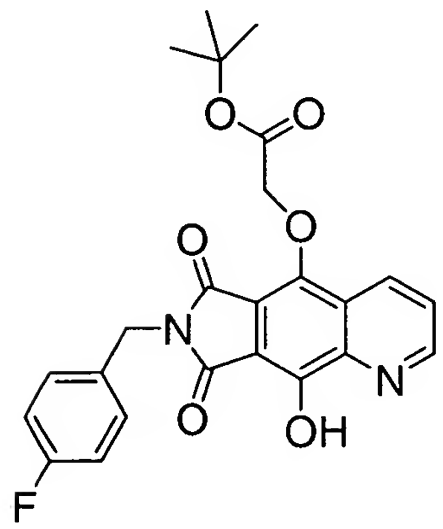

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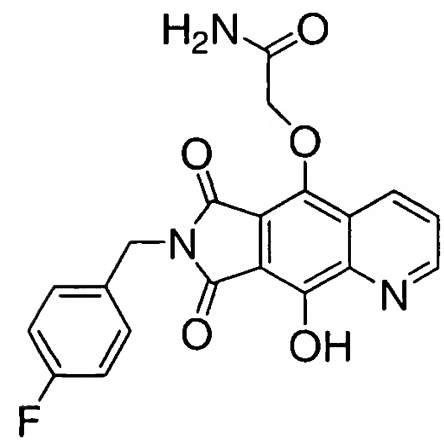

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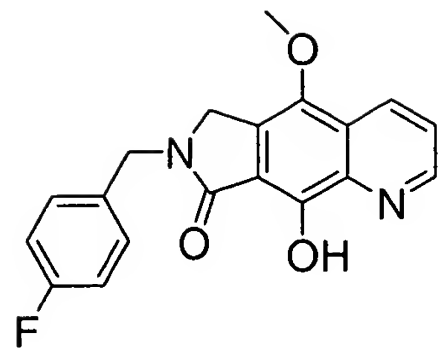

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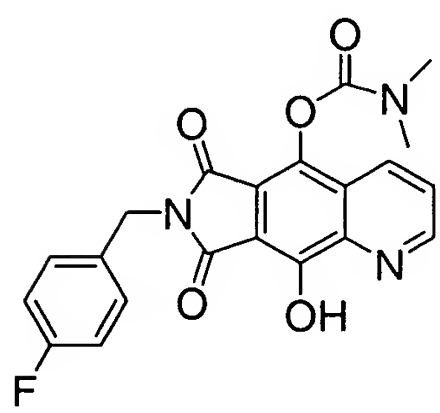

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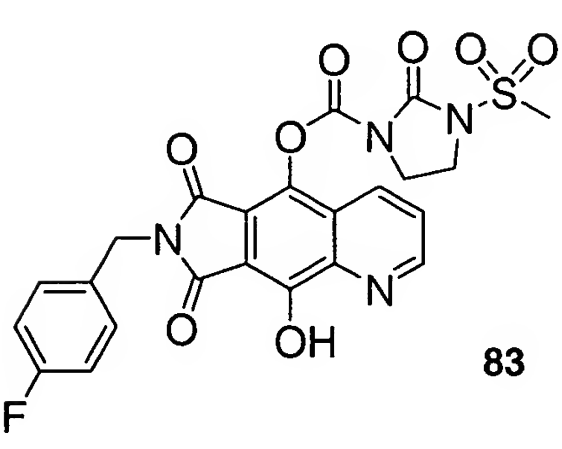

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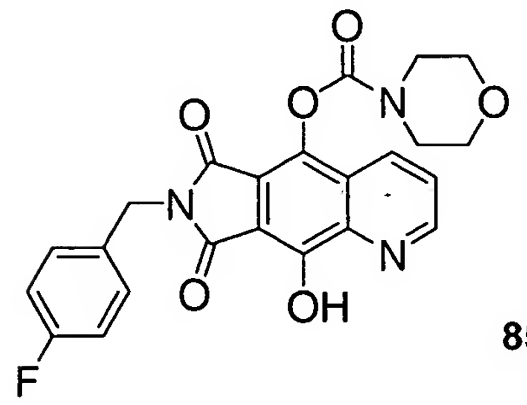

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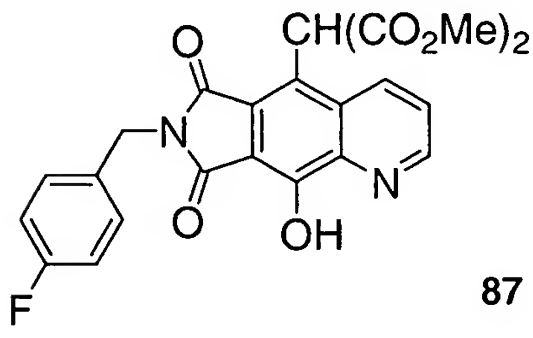

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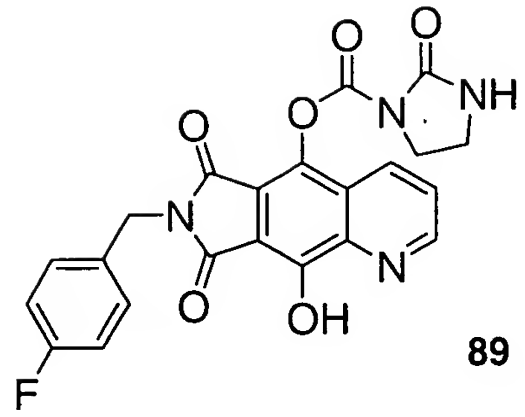

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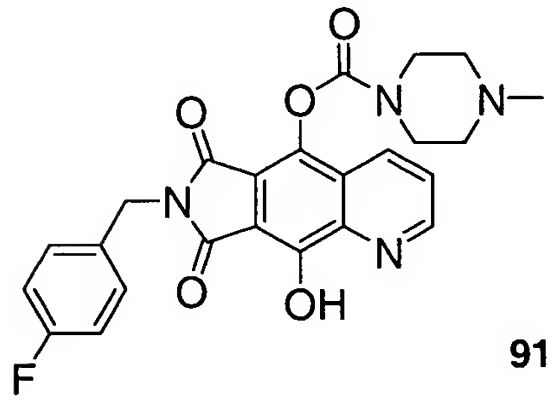

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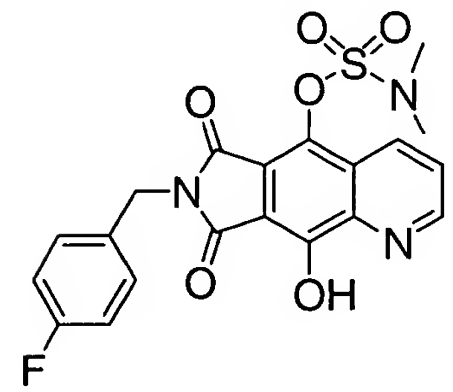

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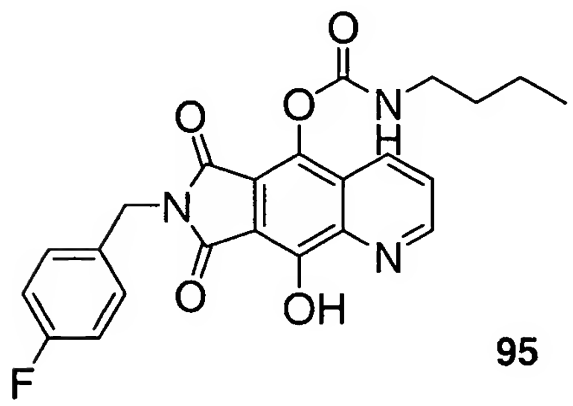

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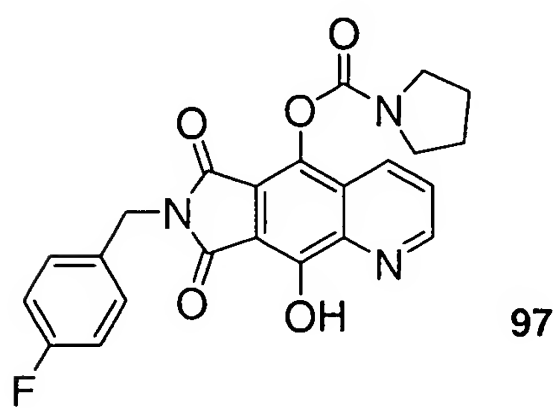

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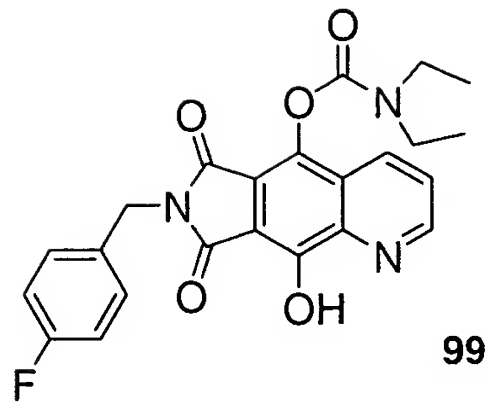

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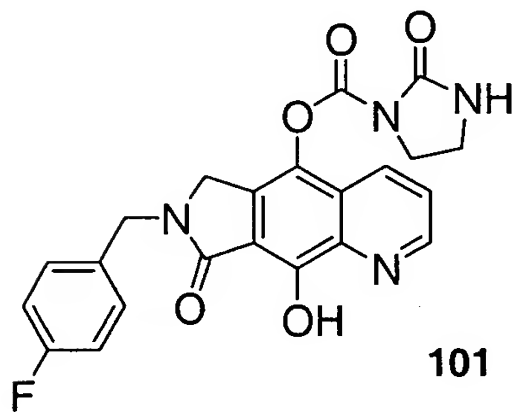

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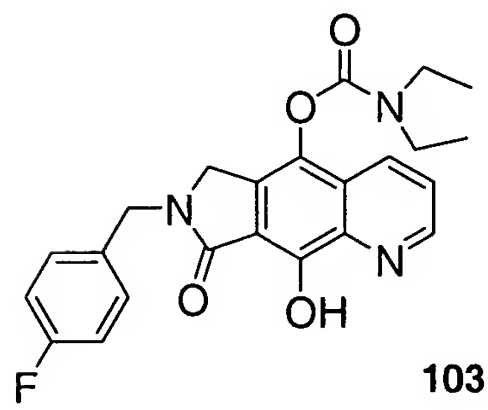

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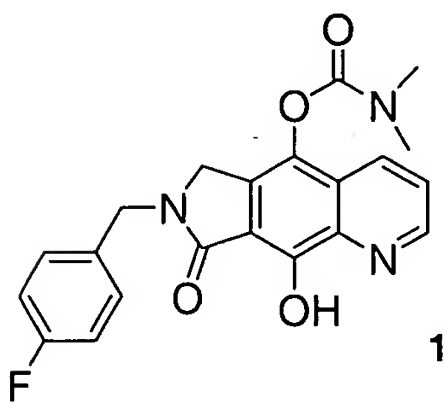

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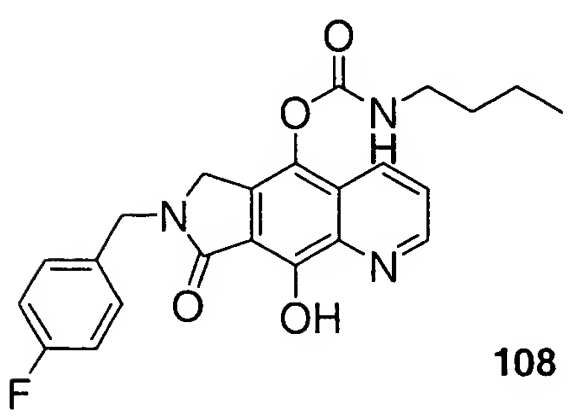

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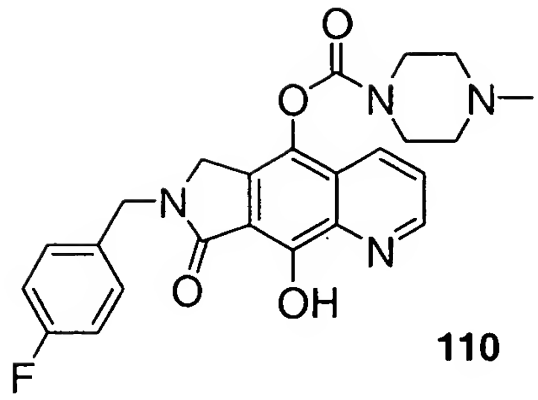

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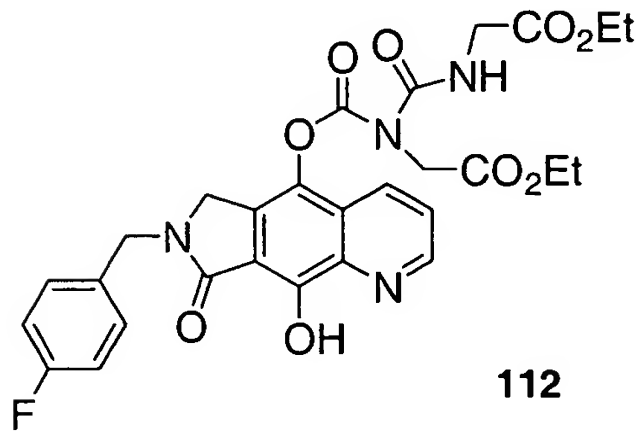

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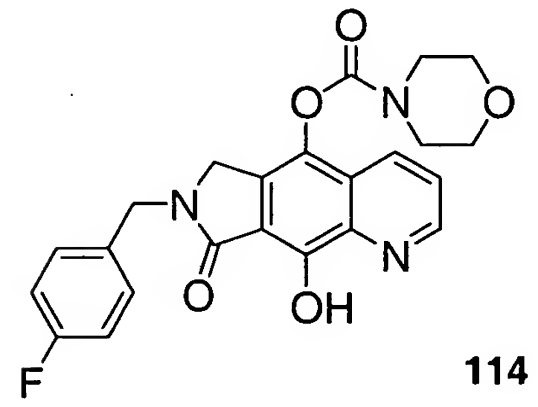

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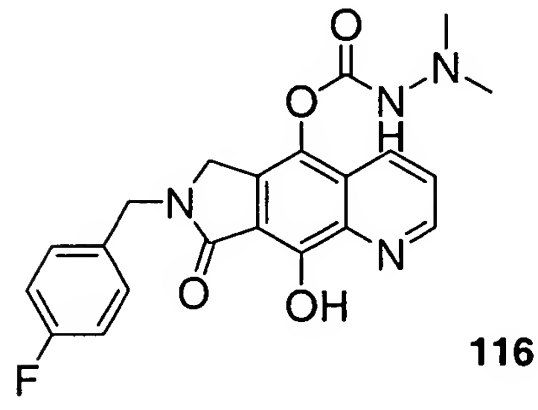

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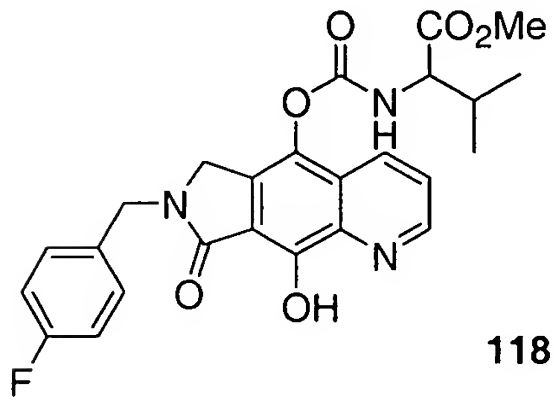

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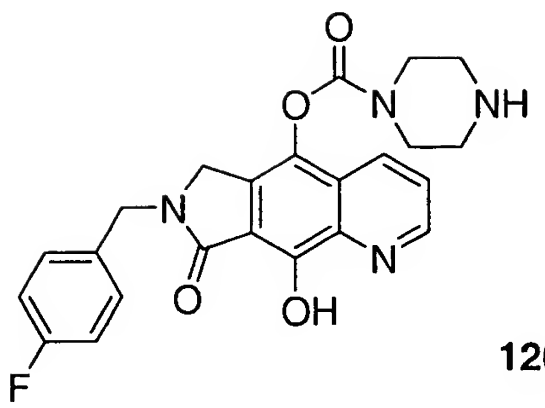

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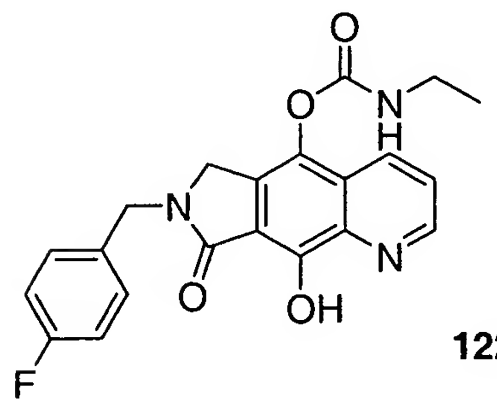

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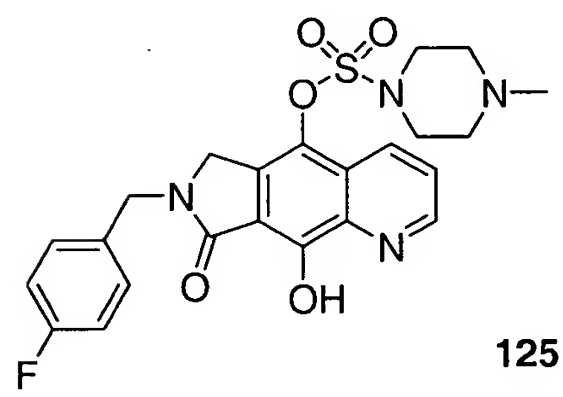

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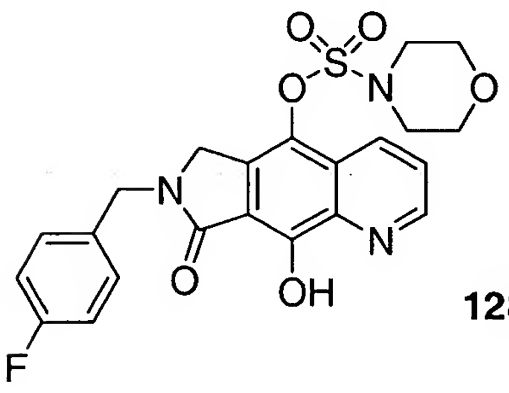

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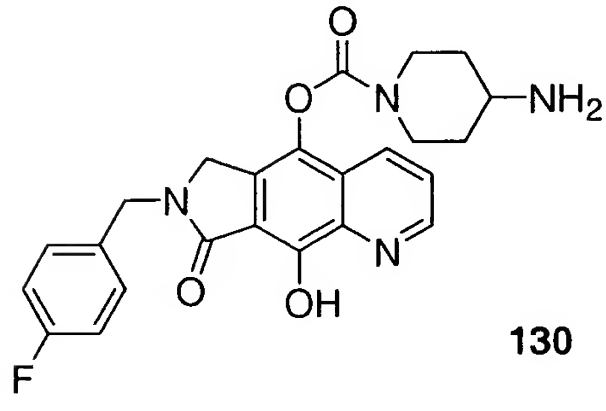

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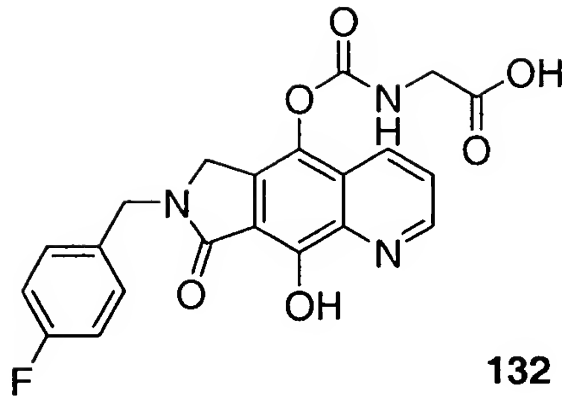

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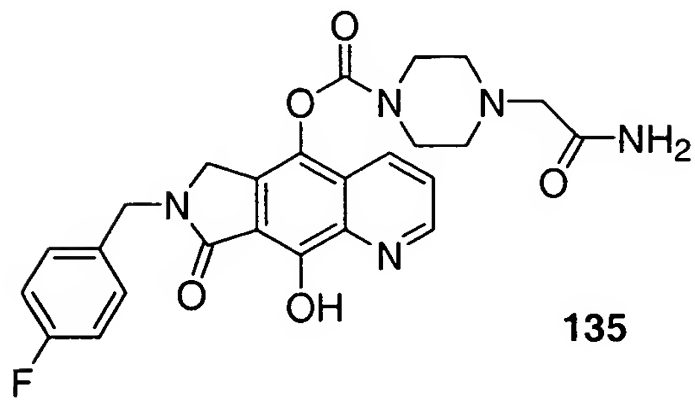

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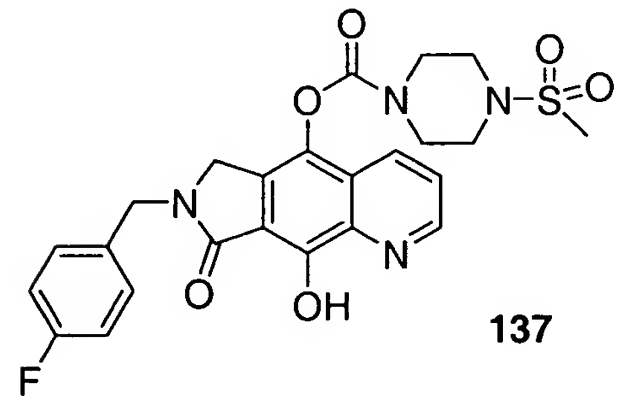

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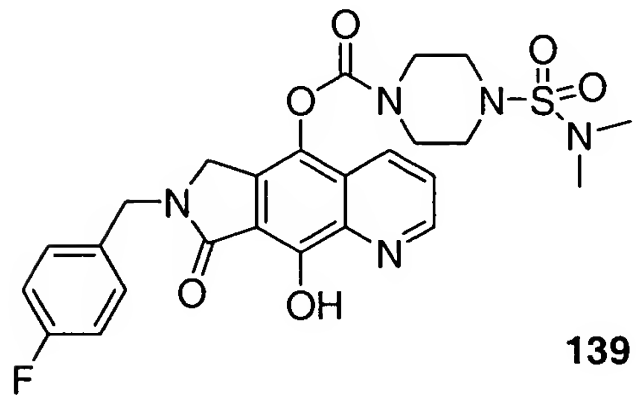

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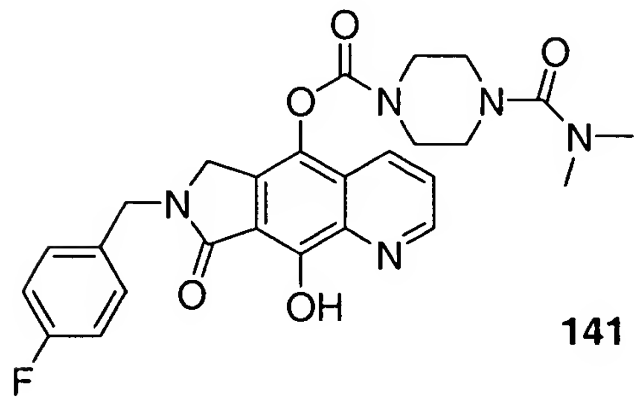

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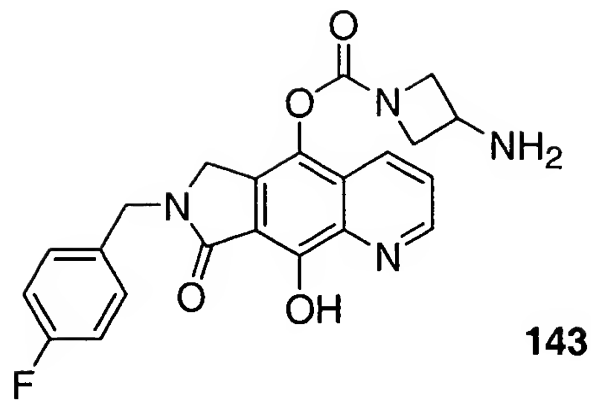

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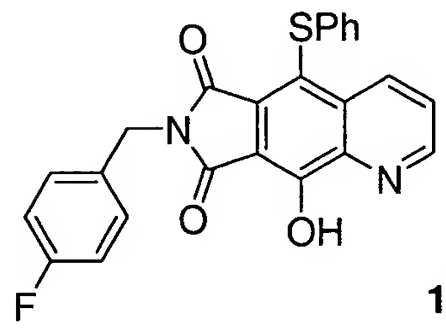

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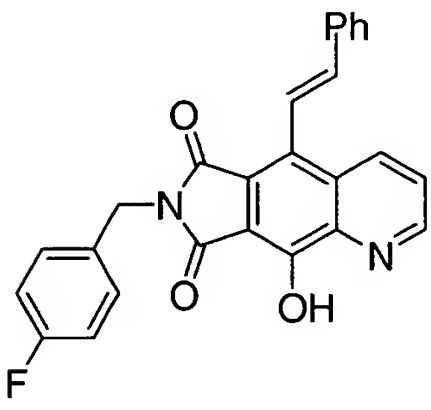

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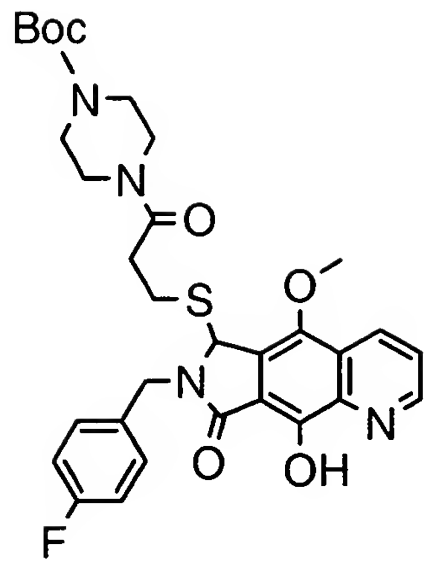

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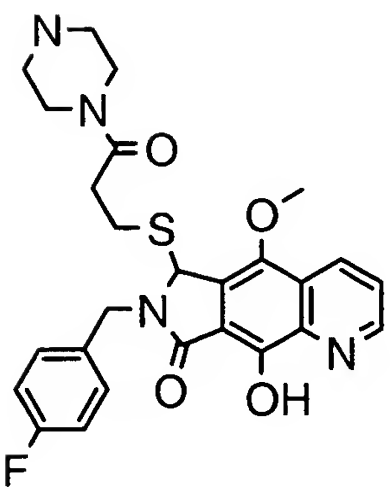

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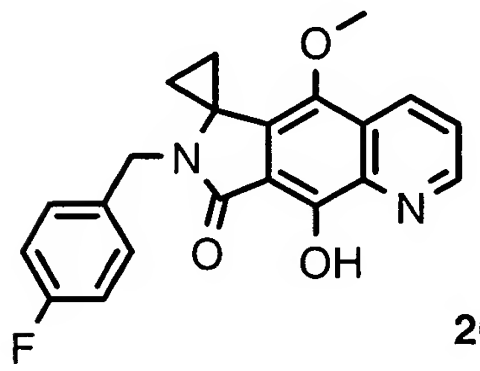

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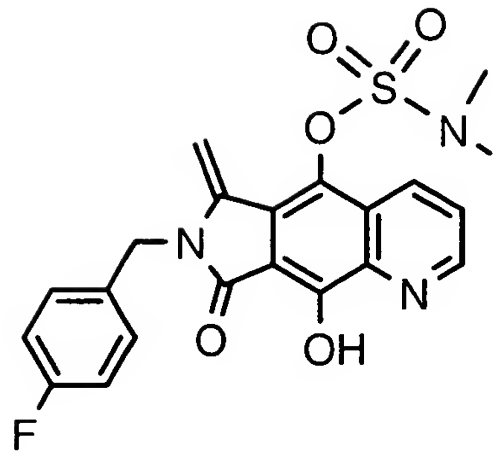

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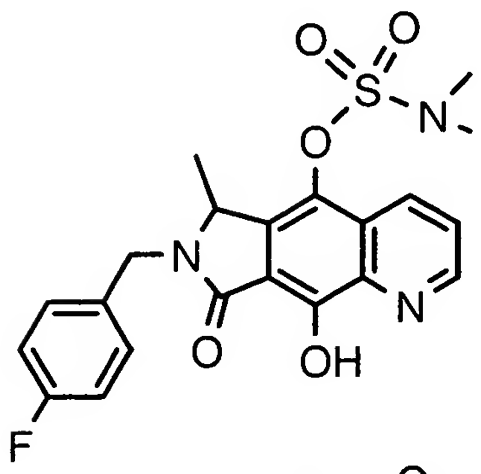

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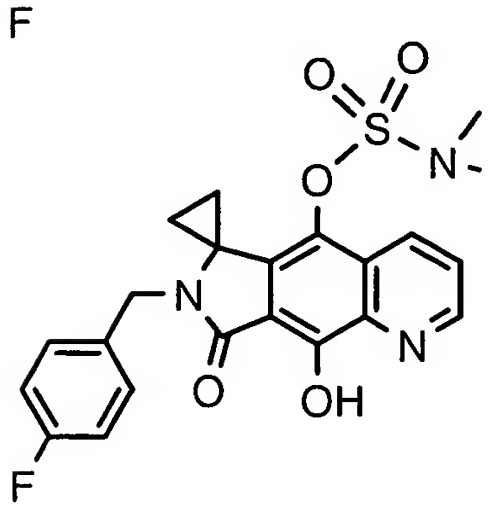

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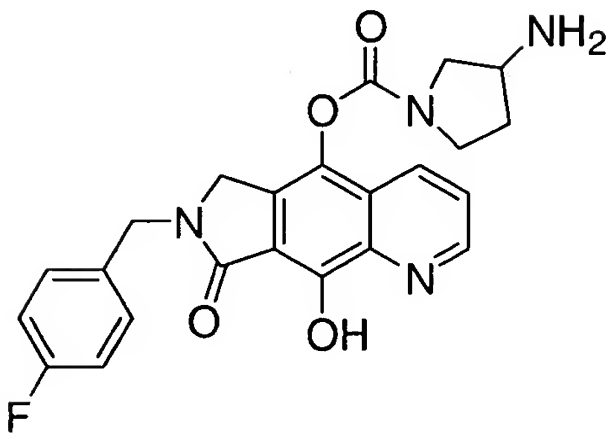

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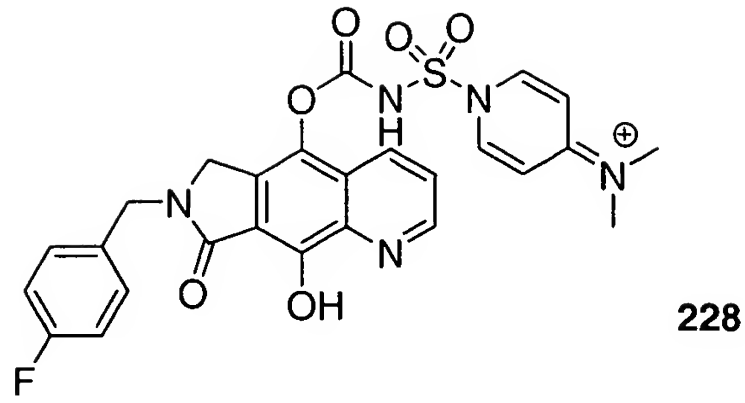

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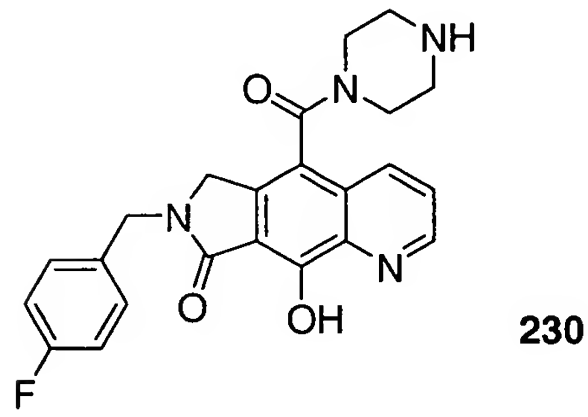

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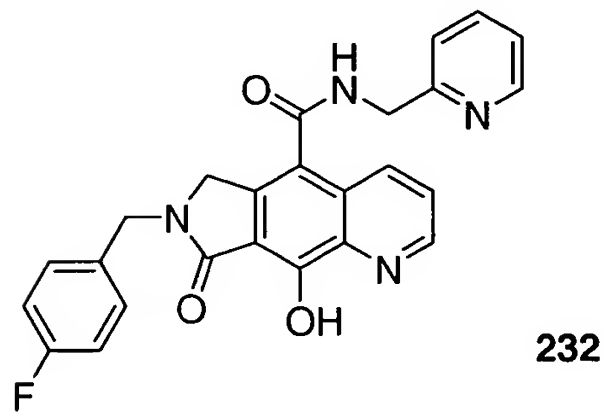

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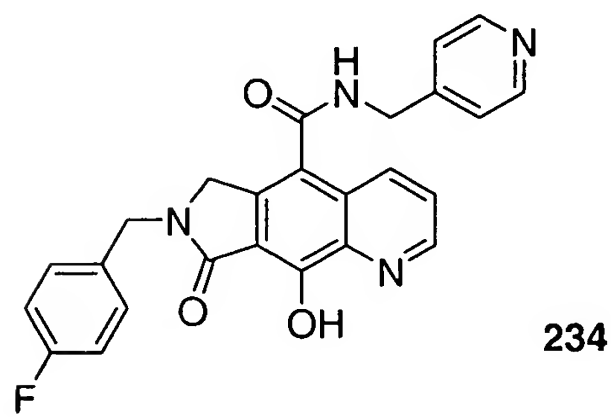

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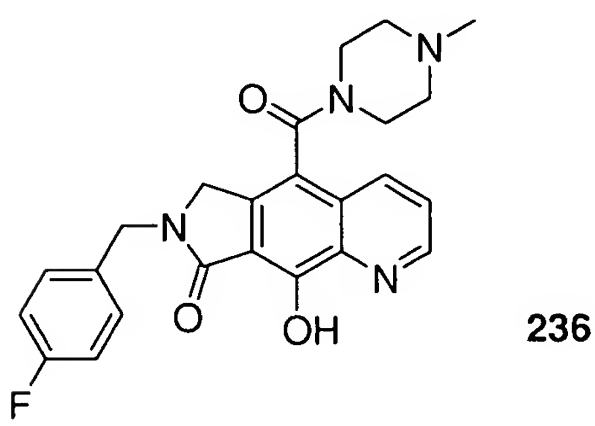

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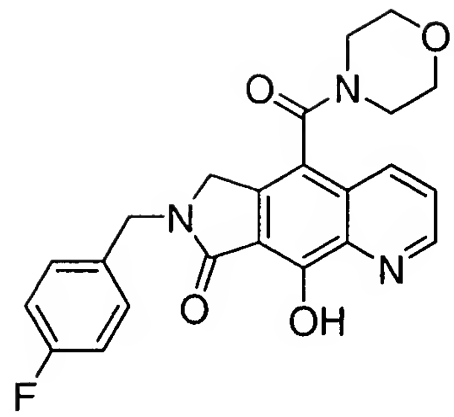

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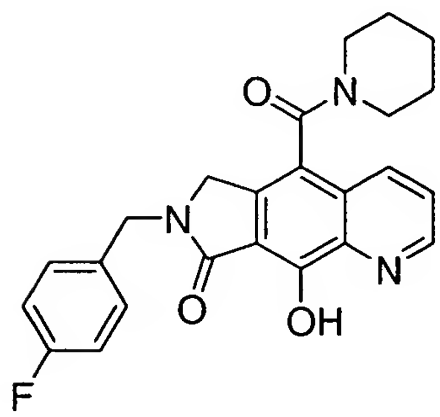

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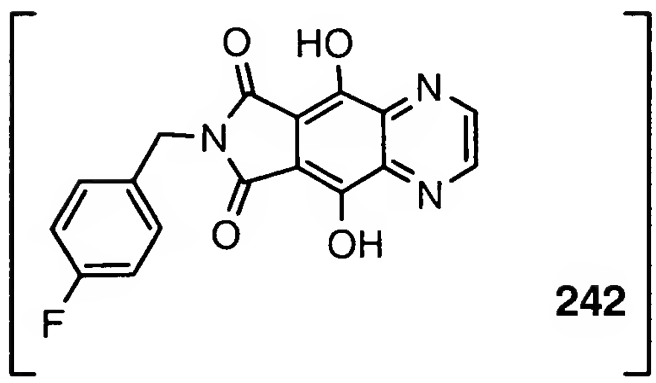

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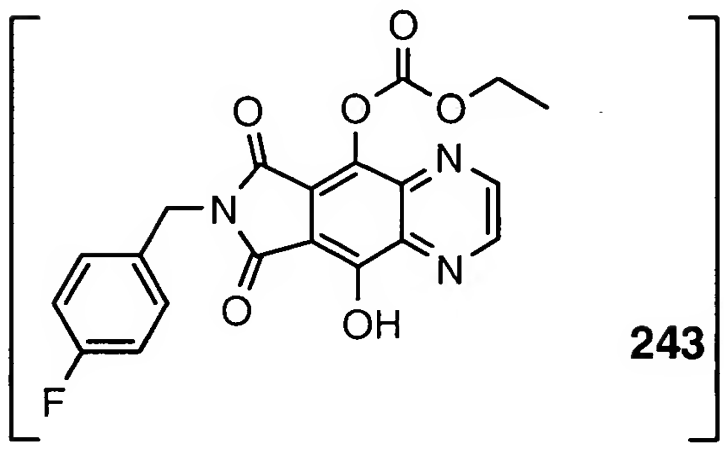

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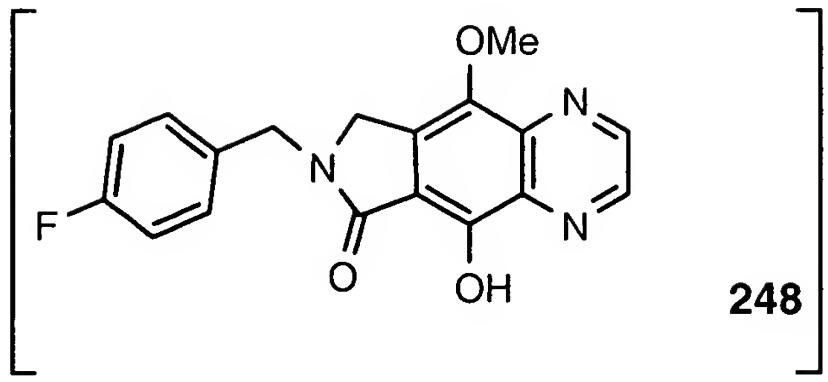

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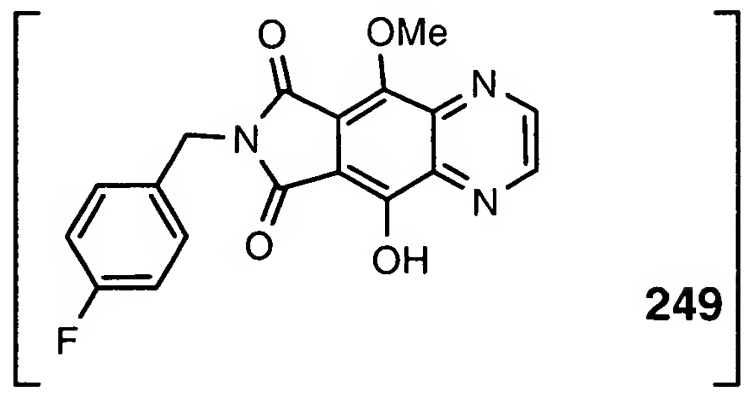

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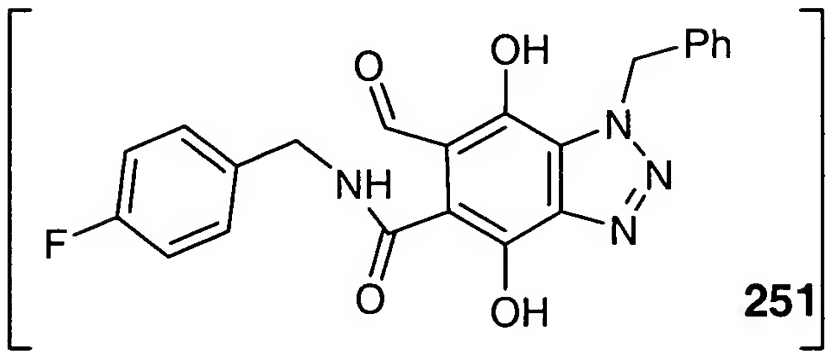

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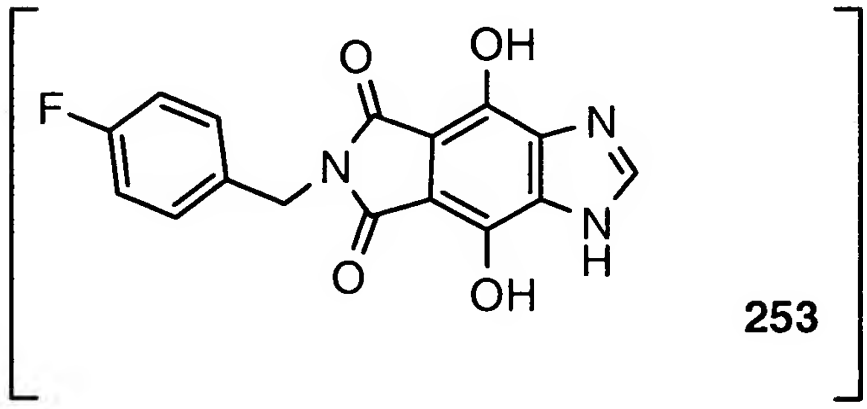

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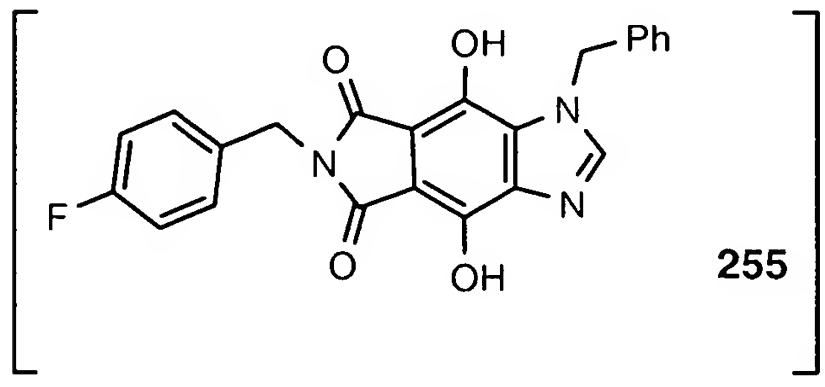

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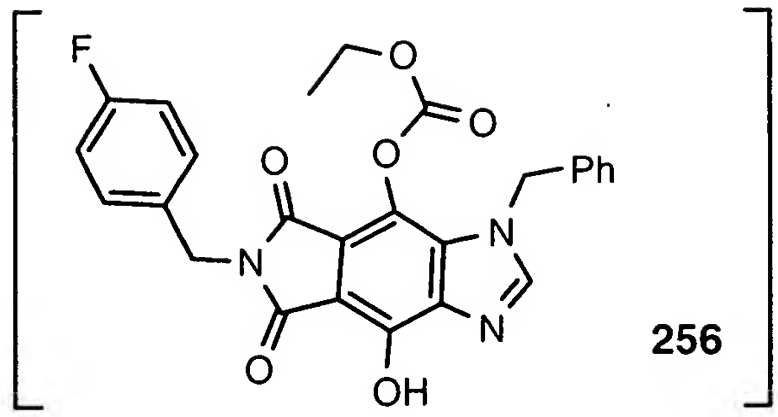

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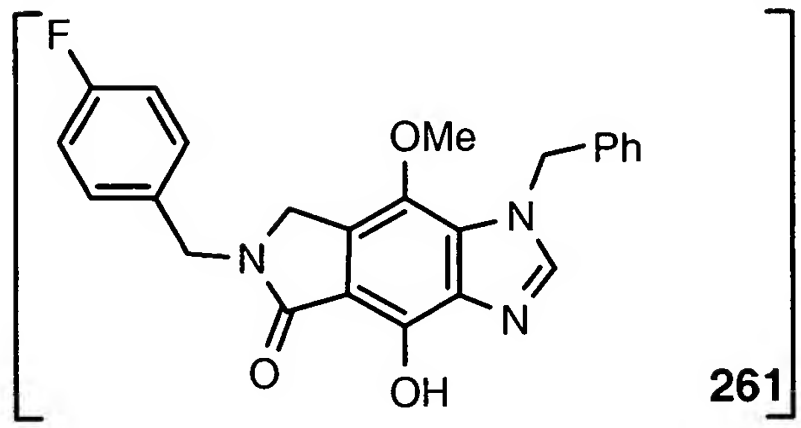

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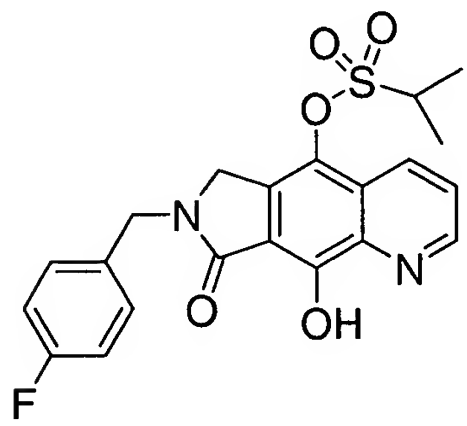

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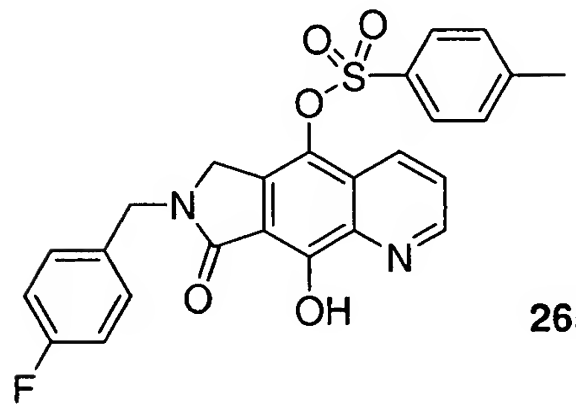

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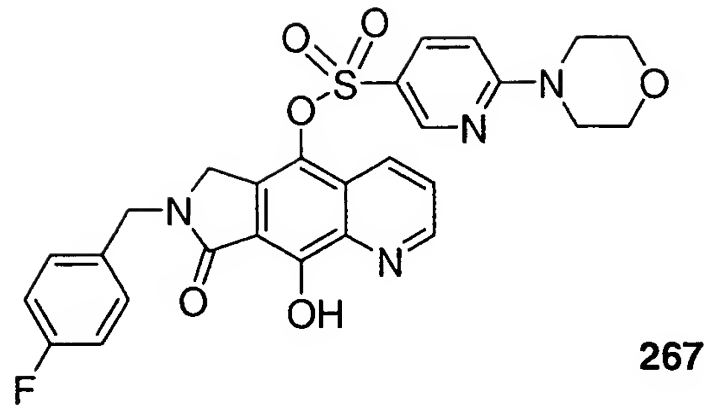

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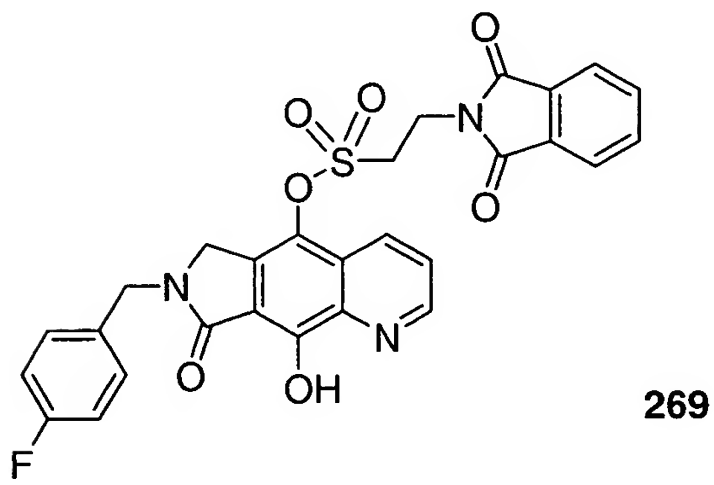

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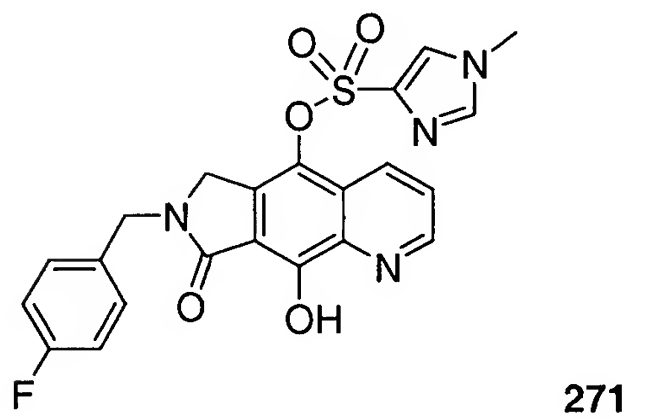

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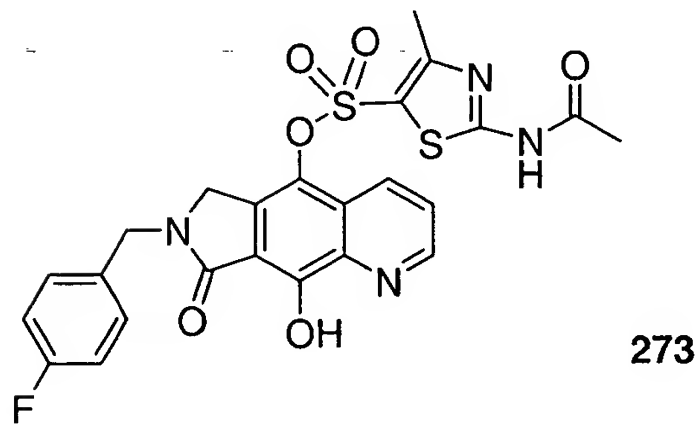

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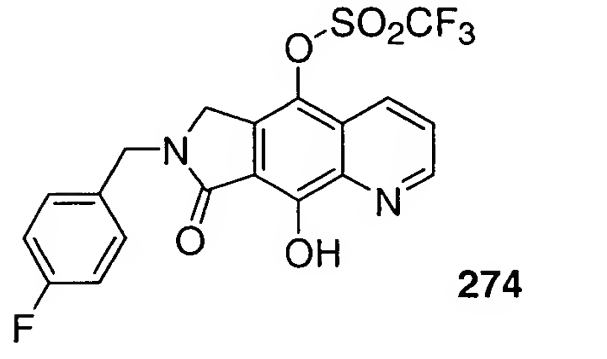

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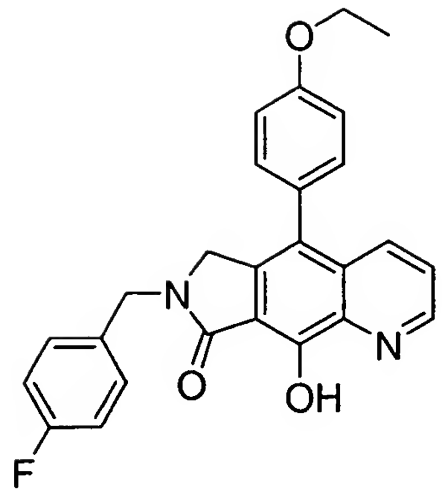

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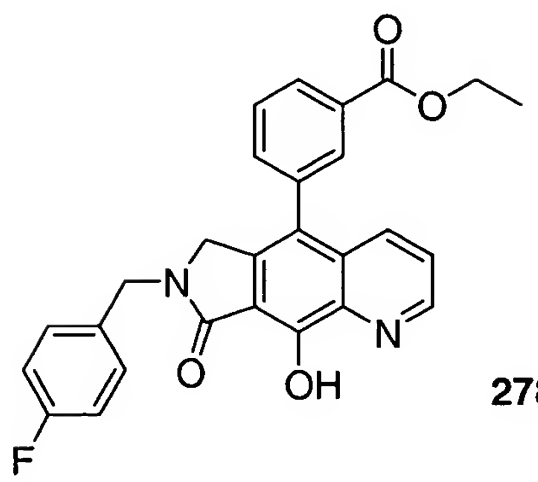

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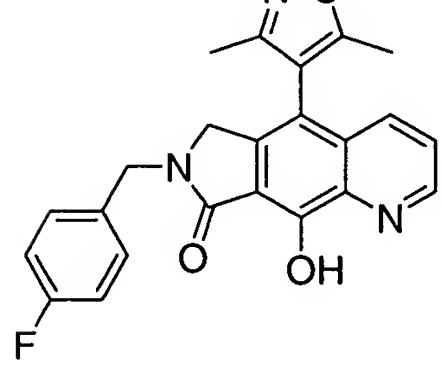

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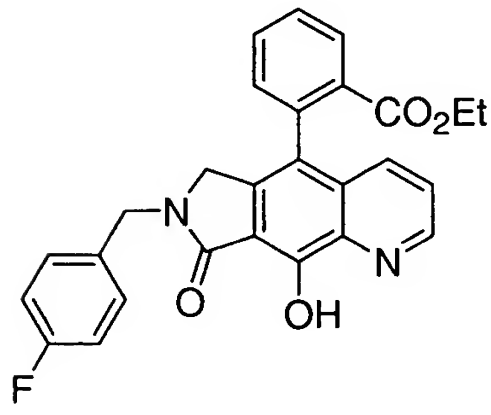

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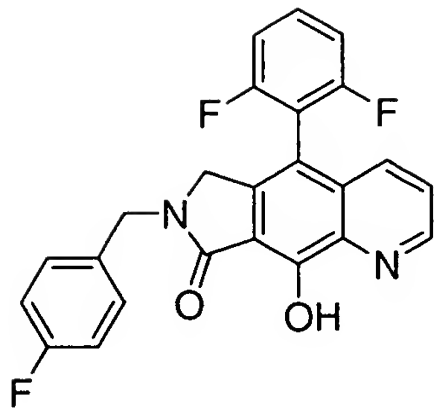

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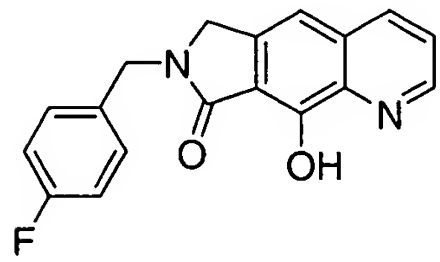

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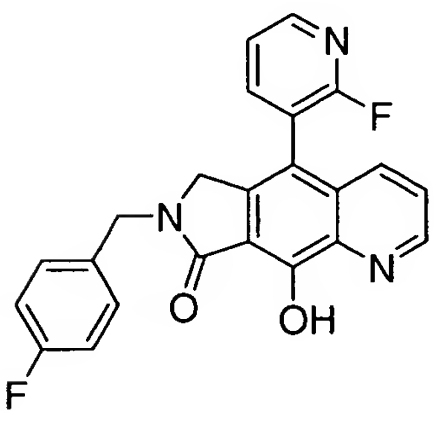

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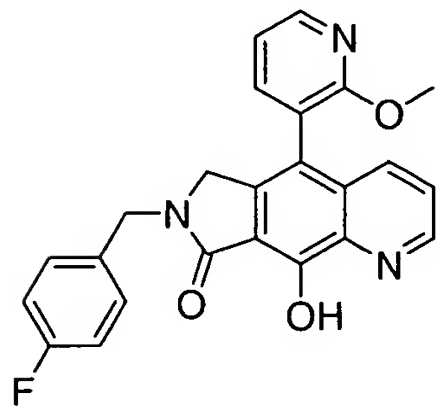

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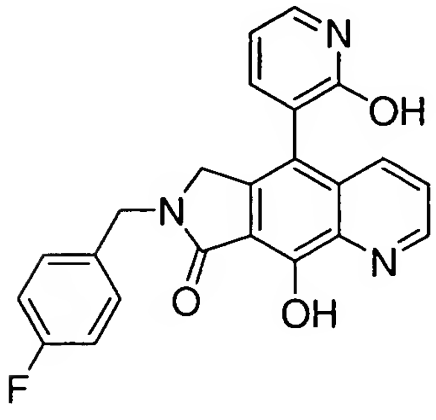

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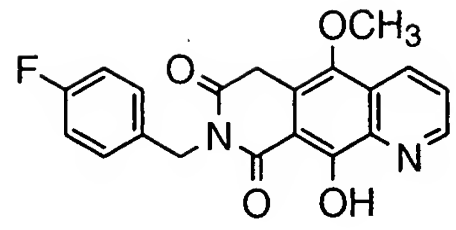

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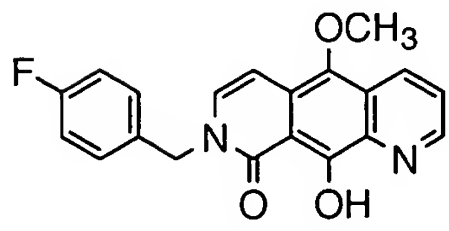

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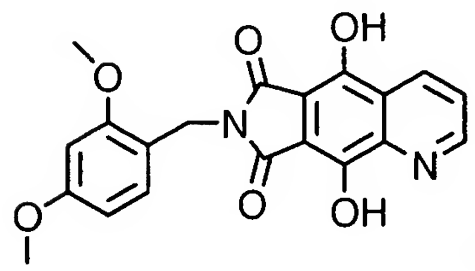

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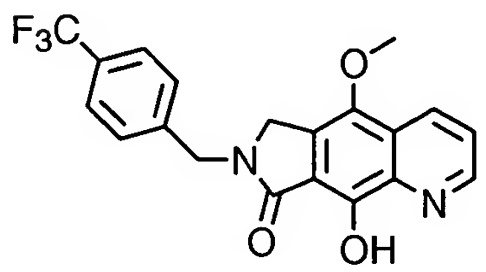

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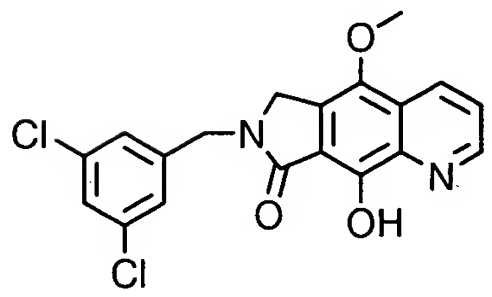

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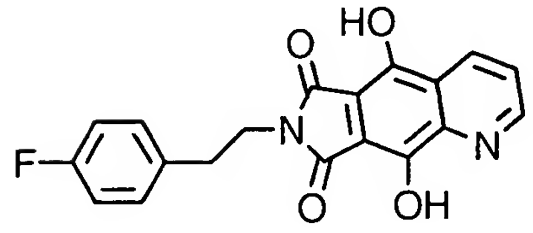

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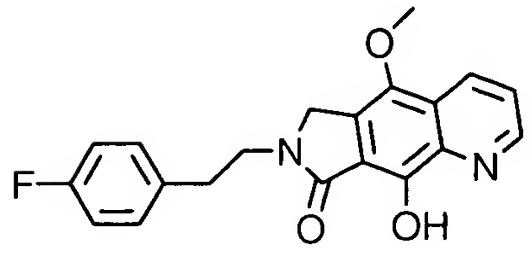

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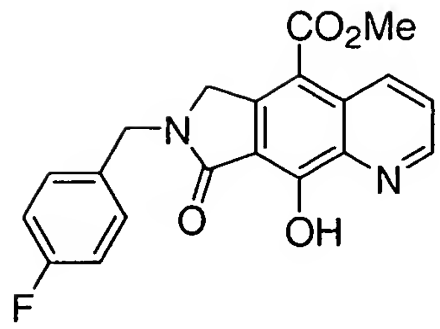

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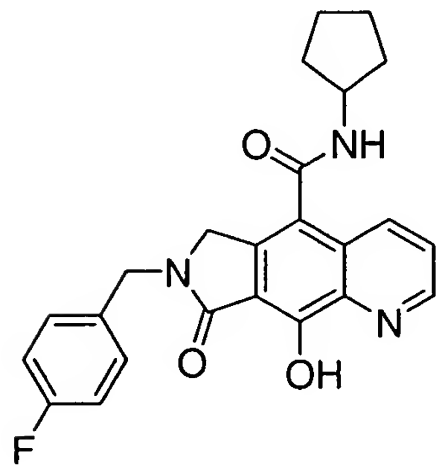

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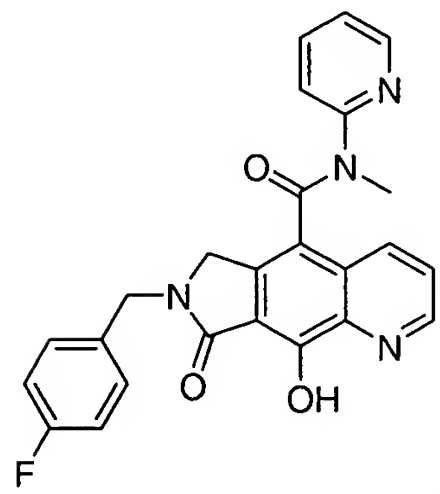

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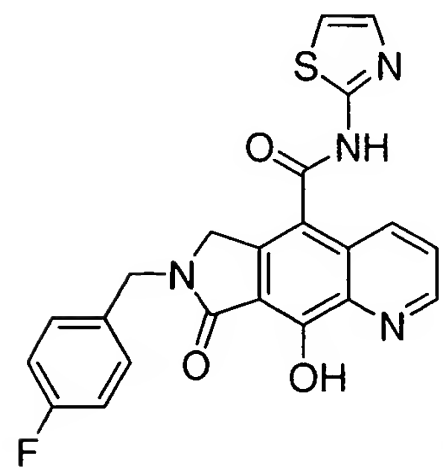

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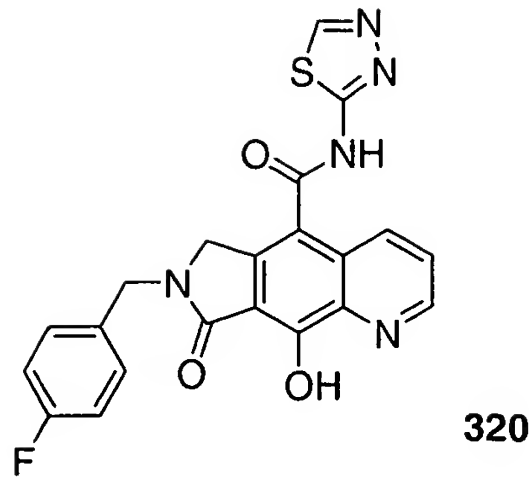

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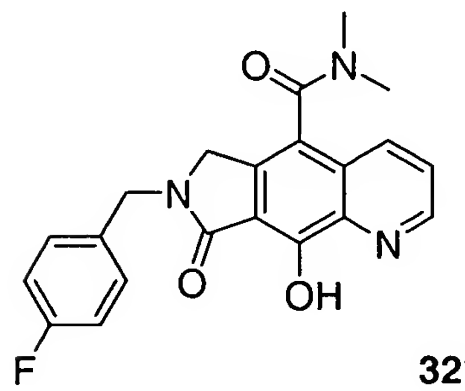

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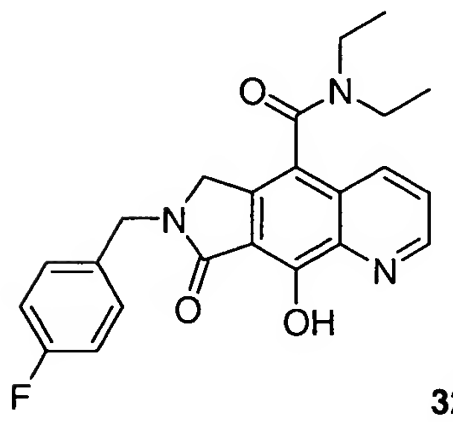
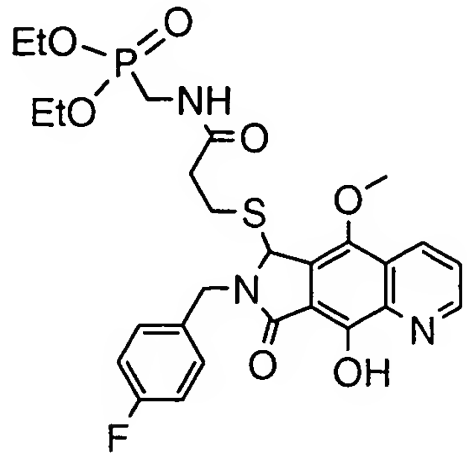
and



322

48. (Currently amended): A compound [of claim 13] selected from the structures:



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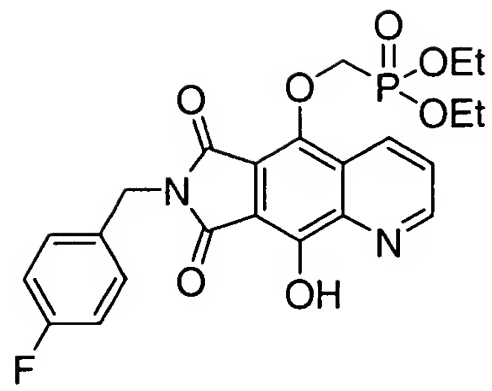

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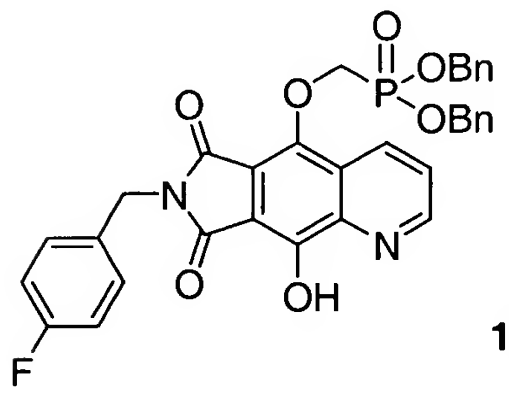

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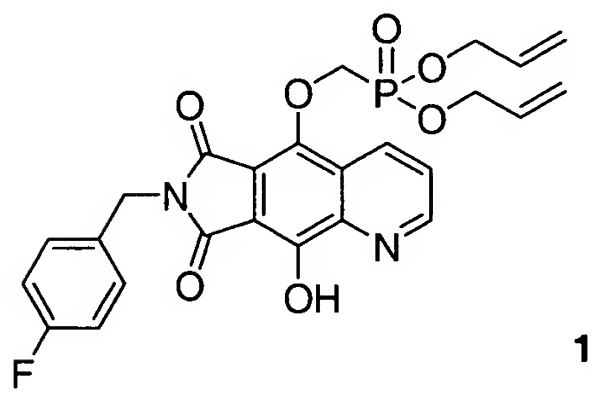

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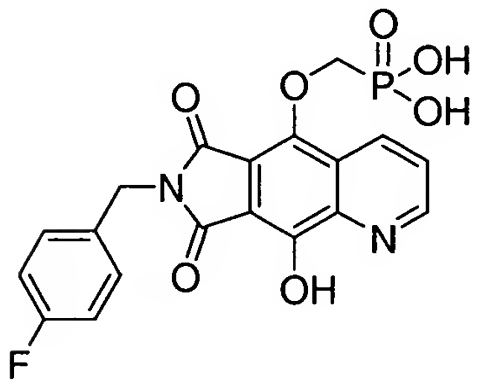

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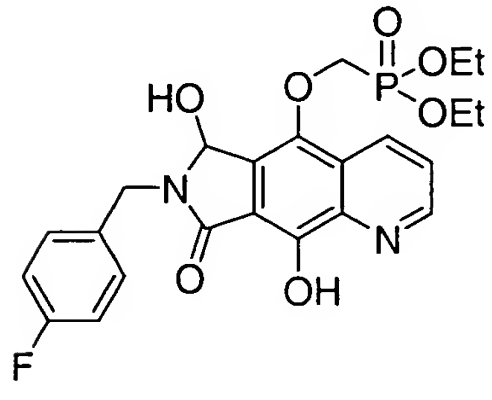

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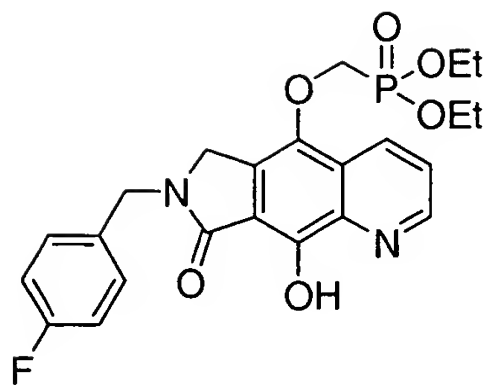

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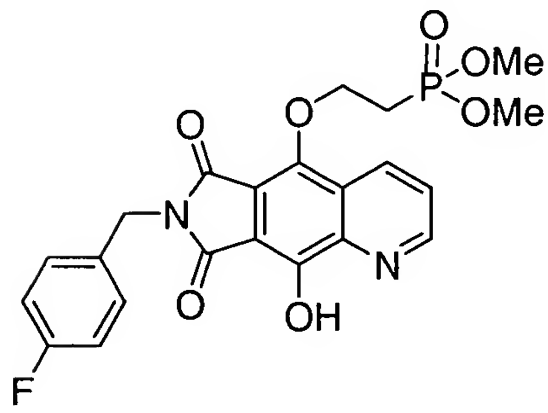

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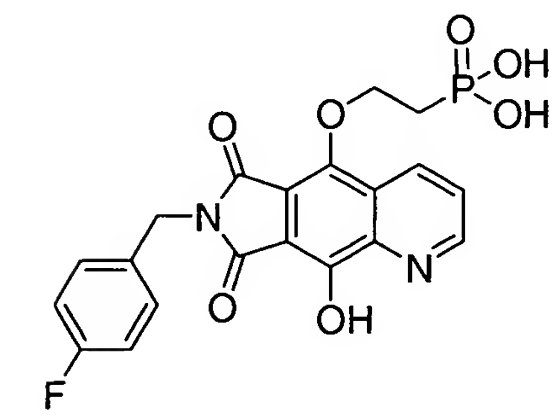

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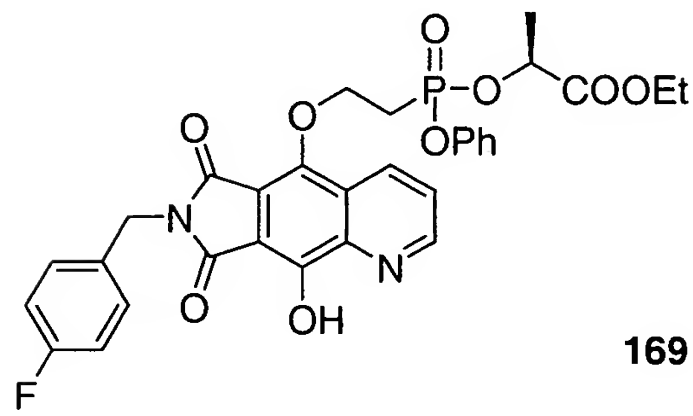

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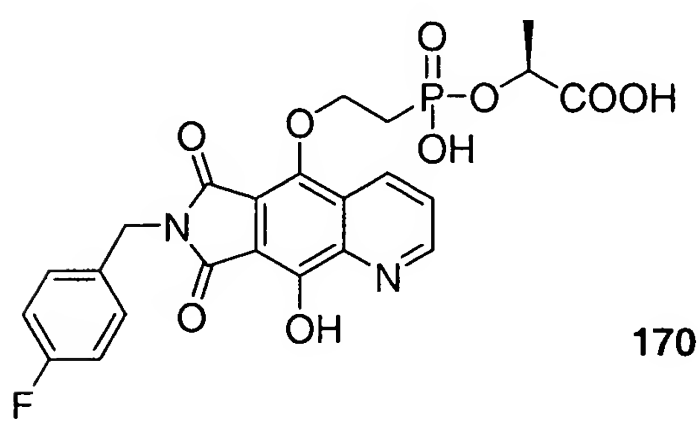

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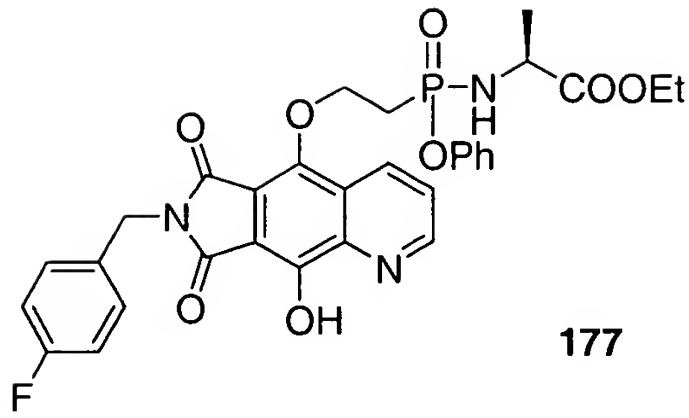

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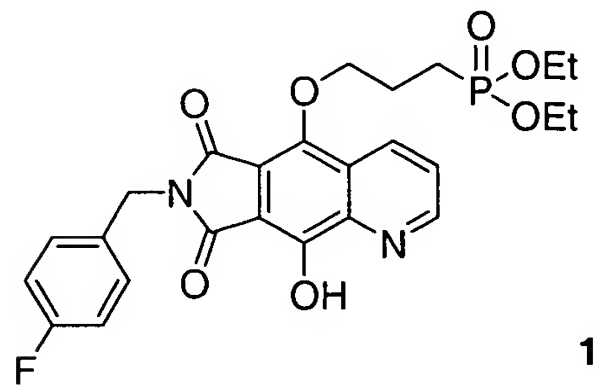

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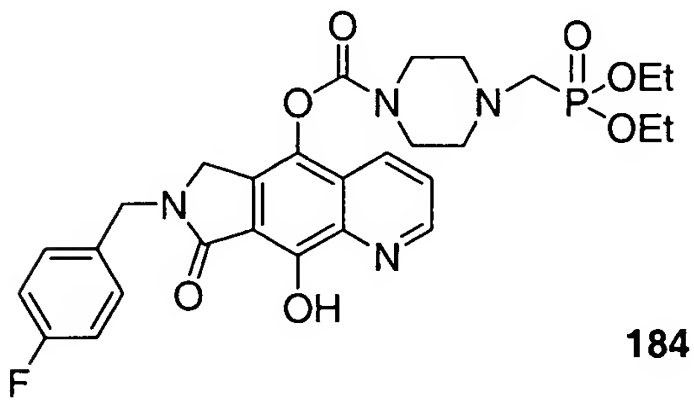

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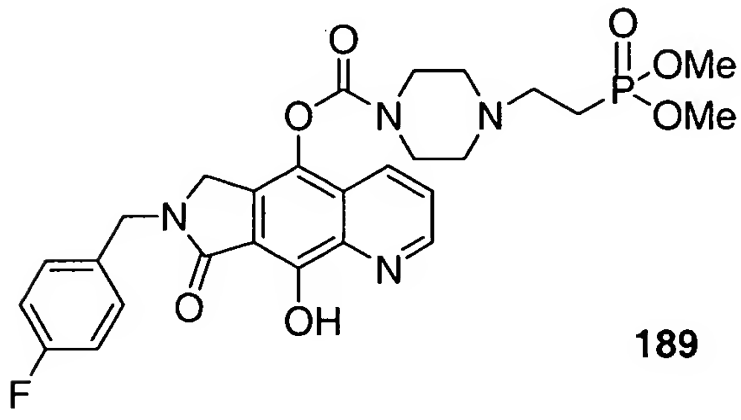

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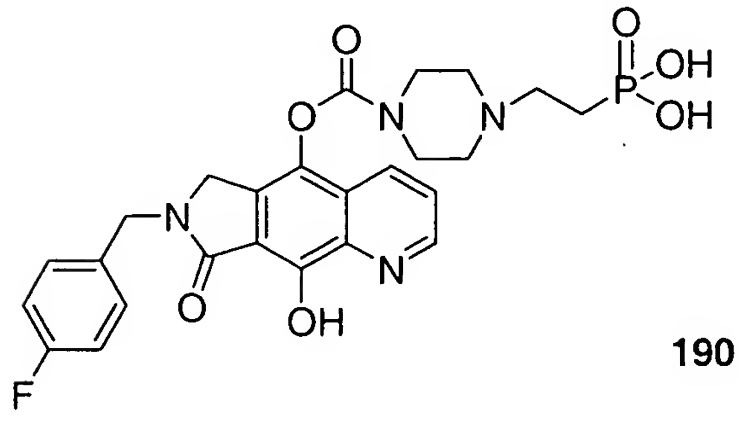

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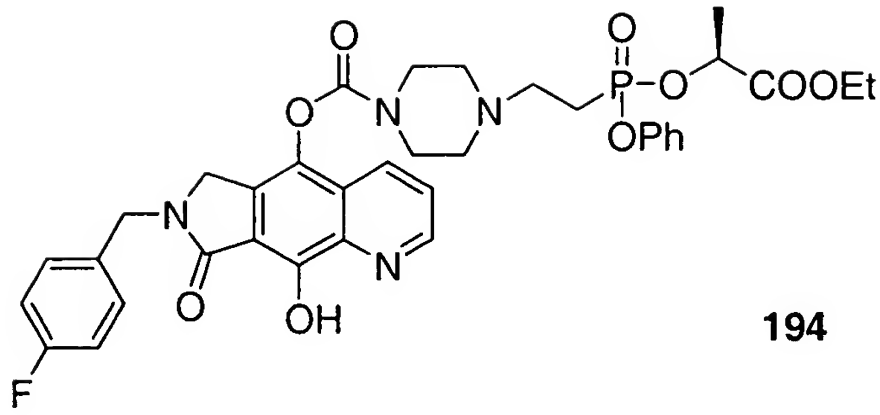

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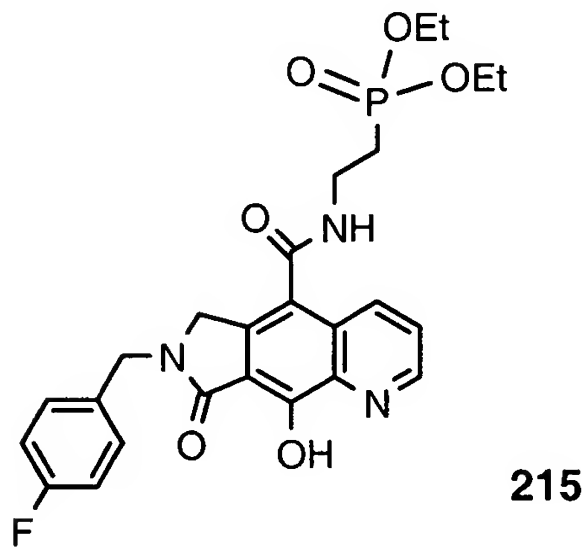

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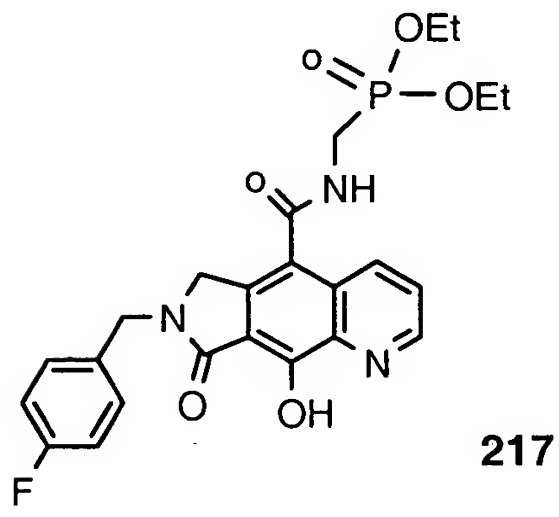

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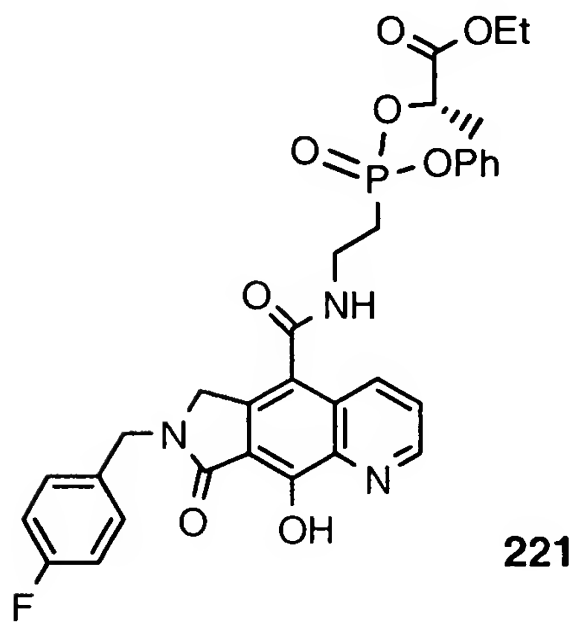

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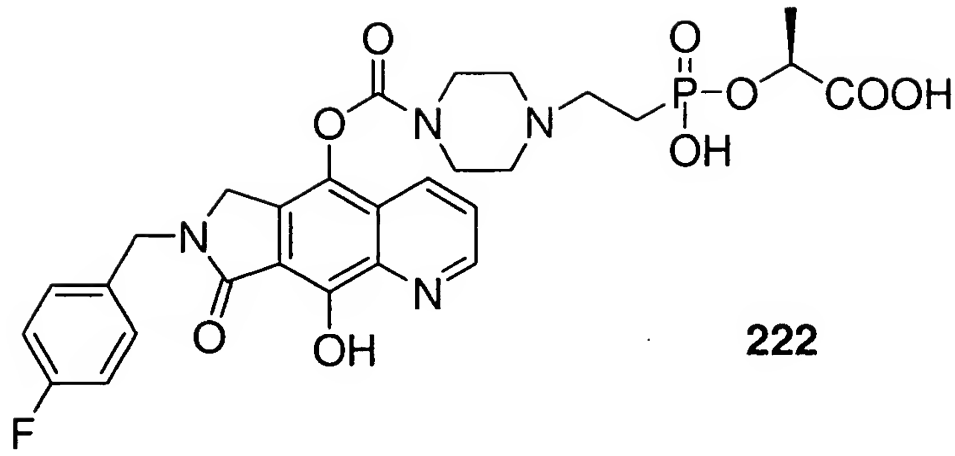

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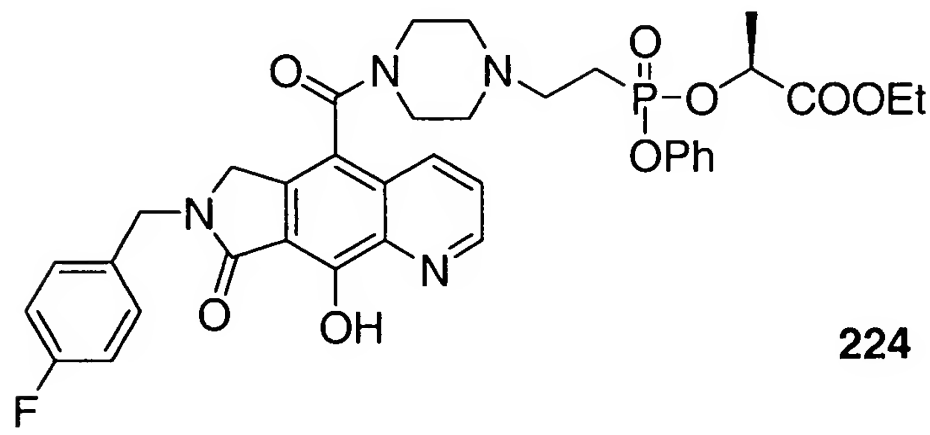

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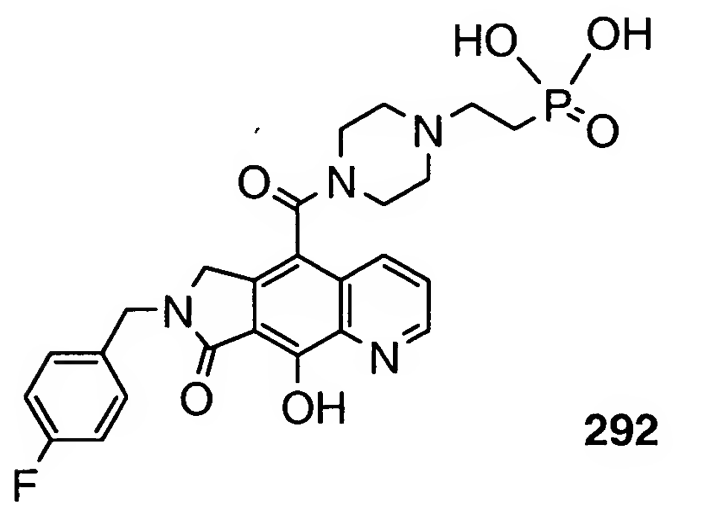

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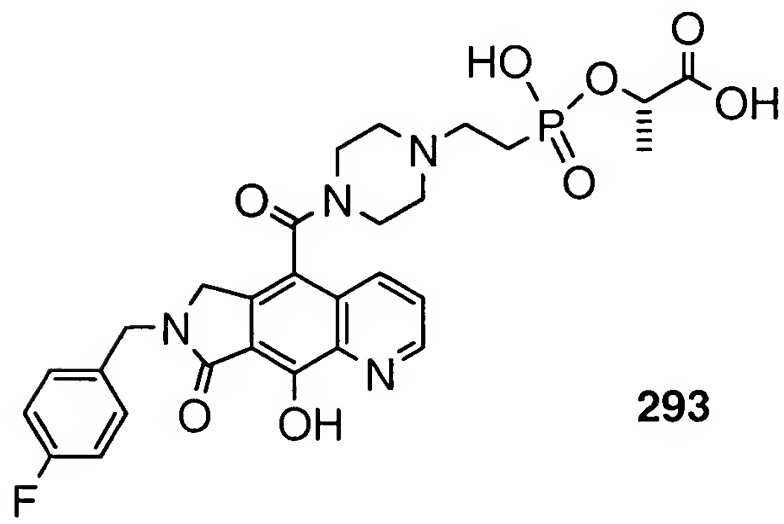

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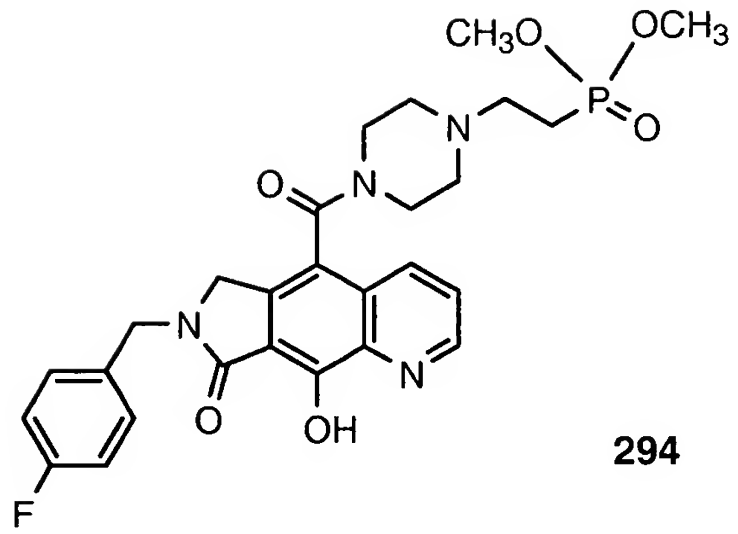

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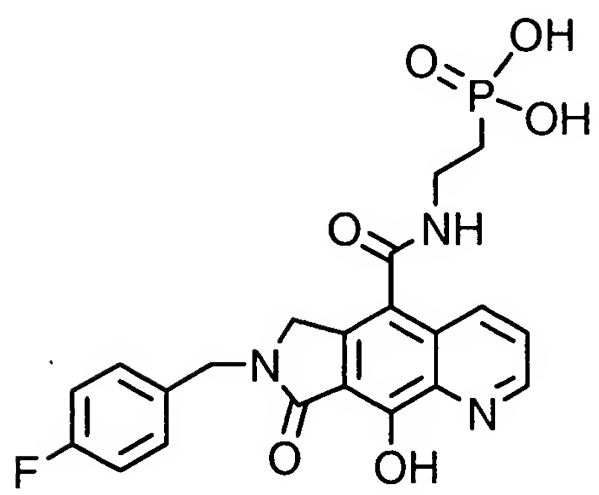
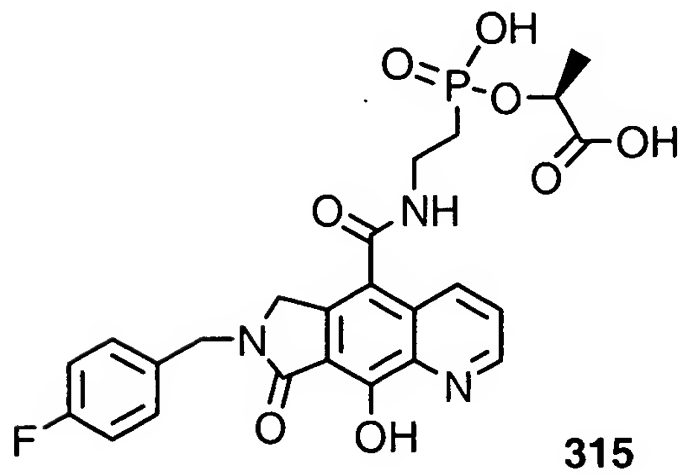


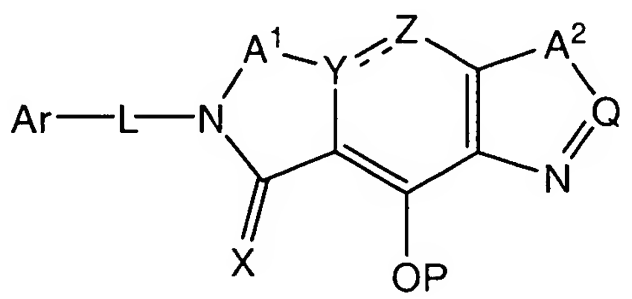
314

and



315

49. (Currently amended): A compound having the structure:



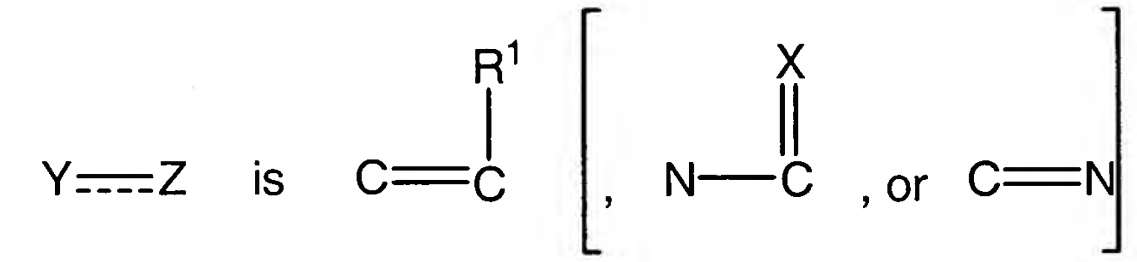
[or a salt thereof;]

wherein:

A^1 [and A^2 are] is independently selected from [O, S, NR,] $C(R^2)_2$, CR^2OR, $CR^2OC(=O)R$, C(=O), C(=S), CR^2SR, and C(=NR),

A^2 is independently selected from $C(R^2)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$, [NR–$C(R^3)_2$, N=$C(R^3)$, N=N, SO_2–NR,] and $C(=O)C(R^3)_{2[}$, C(=O)NR, $C(R^2)_2$–$C(R^3)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$–$C(R^3)_2$, $C(R^2)C(=O)NR$, $C(R^2)C(=S)NR$, $C(R^2)$=N–$C(R^3)_2$, $C(R^2)$=N–NR, and N=$C(R^3)$–NR];

Q is [N, $^+$NR, or] CR^4;

Y⁼⁼⁼Z is  ;

L is selected from a bond, O, S, S–S, S(=O), $S(=O)_2$, $S(=O)_2NR$, NR, N–OR, C_1–C_{12} alkylene, C_1–C_{12} substituted alkylene, C_2–C_{12} alkenylene, C_2–C_{12} substituted alkenylene, C_2–C_{12} alkynylene, C_2–C_{12} substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), $C(=O)NH(CH_2)_n$, or $(CH_2CH_2O)_n$, where n is optionally [may be] 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N–OR, $N–NR_2$, $N–CR_2OR$ and $N–CR_2NR_2$;

Ar is selected from (a) a C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

[R^1,] R^2, R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $–NH_2$, $–NH_3^+$, –NHR, $–NR_2$, $–NR_3^+$, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, $–SO_2R$, $–SO_2Ar$, –SOAr, –SAr, $–SO_2NR_2$, –SOR, $–CO_2R$, $–C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, –CN, $–N_3$, $–NO_2$, C_1–C_8 alkoxy, C_1–C_8 trifluoroalkyl, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate[, and a prodrug moiety];

when taken together on a single carbon, two R^2 or two R^3 may form a spiro ring;

R^1 is independently selected from CR_3, $NRSO_2R$, $OC(=O)NR_2$ $OC(=O)R$, SR, H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, -NHR, $-NR_2$, $-NR_3^+$, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, -SOAr, -SAr, $-SO_2NR_2$, -SOR, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, $-N_3$, $-NO_2$, C_1-C_8 alkoxy, C_1-C_8 trifluoroalkyl, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_3-C_{12} carbocycle, C_3-C_{12} substituted carbocycle, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

R^1 is independently selected from CR_3, $NRSO_2R$, $OC(=O)OR$, $OC(=O)NR_2$ $OC(+O)R$, SR, H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, -NHR, $-NR_2$, $-NR_3^+$, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, -SOAr, -SAr, $-SO_2NR_2$, -SOR, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, $-N_3$, $-NO_2$, C_1-C_8 alkoxy, C_1-C_8 trifluoroalkyl, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_3-C_{12} carbocycle, C_3-C_{12} substituted carbocycle, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

R is independently selected from H, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

R^{X2} is independently selected from H, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate;

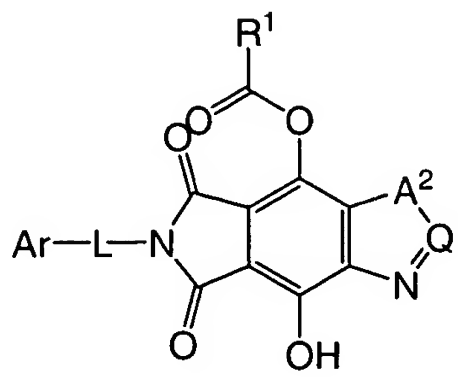
and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof;

with the proviso that when Y=Z is C=C(OH), X is O, A^1 is C(=O), A^2 is $C(R^2)=C(R^3)$, and Q is CH, then L is not a bond.

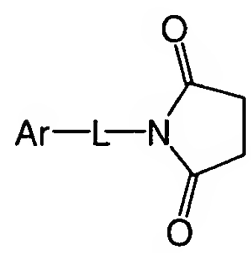
[R is independently selected from H, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, and phosphate, and a prodrug; and

P is a protecting group selected from benzyhydryl ($CHPh_2$), trialkylsilyl (R_3Si), 2-trimethylsiloxyethyl, alkoxymethyl (CH_2OR), and ester ($C(=O)R$)].

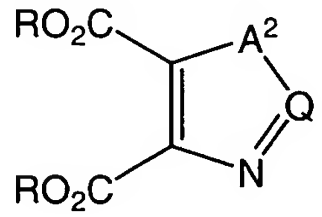
50. (Currently amended): A process for preparation of a compound having the structure:



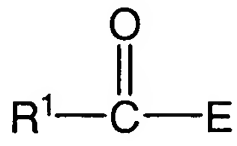
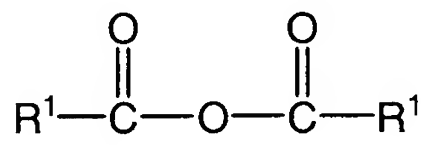
comprising reacting a succinimide compound having the structure:



with a heterocyclic compound having the structure:



and [reaction] reacting with an acylation reagent having [comprising] a formula selected from:

 and 

wherein:

A^2 is selected from [O, S, NR, $C(R^2)_2$, CR^2OR, $CR^2OC(=O)R$, $C(=O)$, $C(=S)$, CR^2SR, $C(=NR)$,] $C(R^2)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$, [NR–$C(R^3)_2$, N=$C(R^3)$, N=N, SO_2–NR,] and $C(=O)C(R^3)_2$, [C(=O)NR, $C(R^2)_2$–$C(R^3)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$–$C(R^3)_2$, $C(R^2)C(=O)NR$, $C(R^2)C(=S)NR$, $C(R^2)$=N–$C(R^3)_2$, $C(R^2)$=N–NR, and N=$C(R^3)$–NR];

Q is [N, $^+$NR, or] CR^4;

L is selected from a bond, O, S, NR, N–OR, C_1–C_{12} alkyldiyl, C_1–C_{12} substituted alkyldiyl, C(=O)NH, C(=O), S(=O), $S(=O)_2$, $C(=O)NH(CH_2)_n$, and $(CH_2CH_2O)_n$, where n ranges from 1 to 6;

Ar is selected from (a) a C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

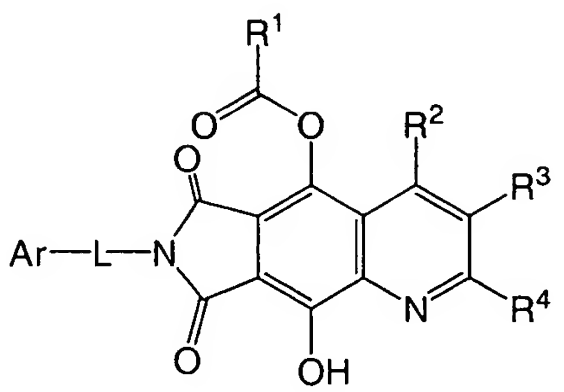
R^1 is selected from R, OR, NR_2, NHR, $NHSO_2R$, and $NRSO_2R$;

E is selected from Cl, imidazole, and hydroxybenzotriazole;

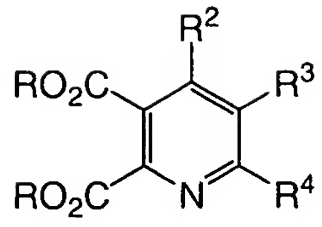
R^2, R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, –NHR, $-NR_2$, $-NR_3^+$, C_1–C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1–C_8 alkylsulfonate, C_1–C_8 alkylamino, 4-dialkylaminopyridinium, C_1–C_8 alkylhydroxyl, C_1–C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, –SOAr, –SAr, $-SO_2NR_2$, –SOR, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, –CN, $-N_3$, $-NO_2$, C_1–C_8 alkoxy, C_1–C_8 trifluoroalkyl, C_1–C_8 alkyl, C_1–C_8 substituted alkyl, C_3–C_{12} carbocycle, C_3–C_{12} substituted carbocycle, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

R is selected from C_1–C_6 alkyl, C_1–C_6 substituted alkyl, C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, C_2–C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

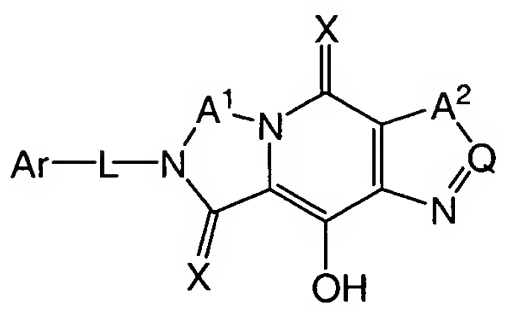
51. (previously presented): The process of claim 50 for preparation of a compound having the structure:



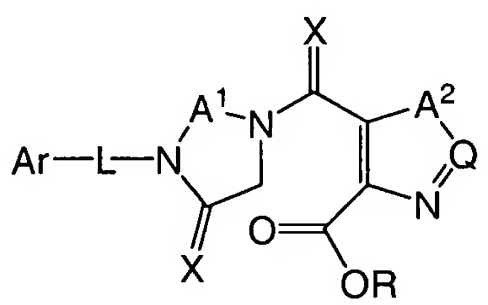
wherein the heterocyclic compound has the structure:



52. (Currently amended): A process for preparation of a compound having the structure:



comprising reacting a compound having the structure:



with a basic reagent comprising hydroxide, an alkoxide or an amine;

wherein:

A^1 [and A^2 are] is independently selected from [O, S, NR,] $C(R^2)_2$, CR^2OR, $CR^2OC(=O)R$, C(=O), C(=S), CR^2SR, and C(=NR),

A^2 is independently selected from $C(R^2)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$, [$C(R^2)_2$–O, NR–$C(R^3)_2$, N=$C(R^3)$, N=N, SO_2–NR,] and C(=O)$C(R^3)_2$, [C(=O)NR, $C(R^2)_2$–$C(R^3)_2$–$C(R^3)_2$, $C(R^2)$=$C(R^3)$–$C(R^3)_2$, $C(R^2)$C(=O)NR, $C(R^2)$C(=S)NR, $C(R^2)$=N–$C(R^3)_2$, $C(R^2)$=N–NR, and N=$C(R^3)$–NR];

Q is [N, $^+$NR, or] CR^4;

X is selected from O, S, NH, NR, N–OR, N–NR_2, N–CR_2OR and N–CR_2NR_2;

L is selected from a bond, O, S, NR, N–OR, C_1–C_{12} alkyldiyl, C_1–C_{12} substituted alkyldiyl, C(=O)NH, C(=O), S(=O), $S(=O)_2$, C(=O)NH$(CH_2)_n$, and $(CH_2CH_2O)_n$, where n ranges from 1 to 6;

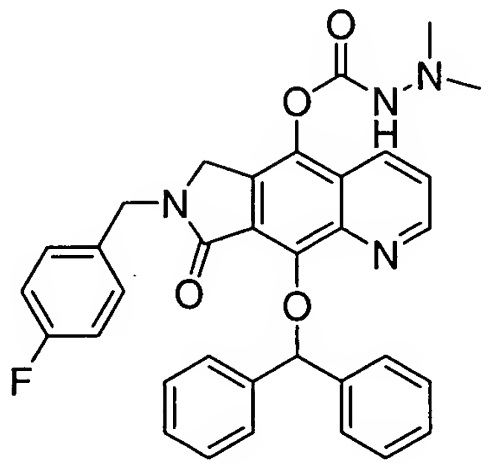
Ar is selected from (a) a C_6–C_{20} aryl, C_6–C_{20} substituted aryl, C_2–C_{20} heteroaryl, and C_2–C_{20} substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

R^2, R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, $-NHR$, $-NR_2$, $-NR_3^+$, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1-C_8 alkoxy, C_1-C_8 trifluoroalkyl, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_3-C_{12} carbocycle, C_3-C_{12} substituted carbocycle, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

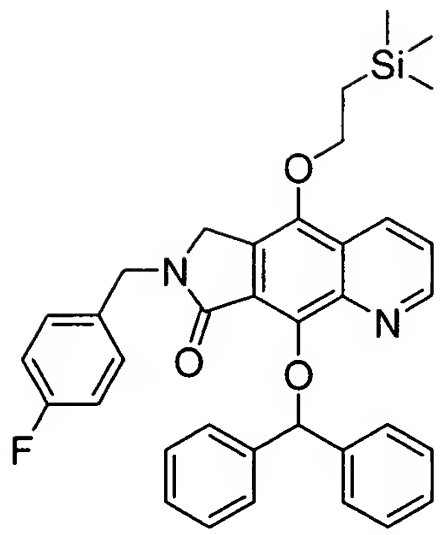
R is selected from C_1-C_6 alkyl, C_1-C_6 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

53. (previously presented): A process for preparation of a compound having structure 115:



115

comprising reacting a compound having the structure 44:



44

with tetrabutylammonium fluoride to form a desilylated intermediate; and

reacting the desilylated intermediate with triphosgene (bis(trichloromethyl) carbonate), followed by dimethylhydrazine to form structure 115.

54. (Currently amended): A compound of claim 1 substituted with [comprising a] phosphonate [prodrug] and capable of accumulating in human PBMC.

55. (previously presented): The compound of claim 54 wherein the intracellular half-life [bioavailability] of the compound or an intracellular metabolite of the compound in human PBMC is increased by at least about 50% [improved] when compared to the analog of the compound not having the phosphonate [or phosphonate prodrug].

56. (canceled)

57. (canceled)

58. (Currently amended): The compound of claim 55 [56] wherein the half-life is improved by at least about 100%.

59. (canceled)

60. (canceled)

61. (canceled)

62. (canceled)

63. (previously presented): A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

64. (previously presented): The pharmaceutical composition of claim [62] 63 further comprising a therapeutically effective amount of an AIDS treatment agent selected from an HIV inhibitor agent, an anti-infective agent, and an immunomodulator.

65. (previously presented): The pharmaceutical composition of claim 64 wherein the HIV inhibitor agent is an HIV-protease inhibitor.

66. (previously presented): The composition of claim 64 wherein the HIV inhibitor agent is a nucleoside reverse transcriptase inhibitor.

67. (previously presented): The composition of claim 64 wherein the HIV inhibitor agent is a non-nucleoside reverse transcriptase inhibitor.

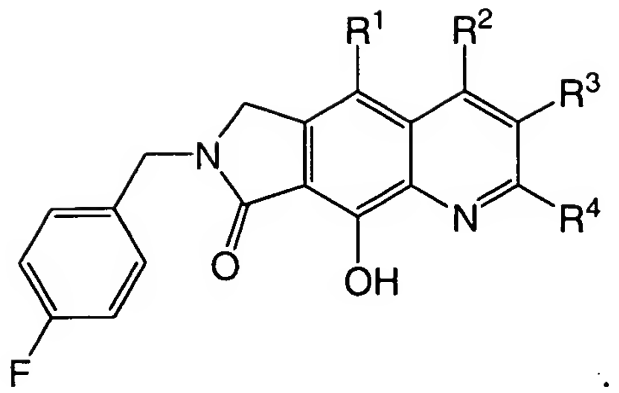
68. (previously presented): A process for making a pharmaceutical composition comprising combining a compound of claim 1 and a pharmaceutically acceptable carrier.

69. (previously presented): A method of inhibiting HIV integrase, comprising the administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.

70. (previously presented): A method of treating infection by HIV, or of treating AIDS or ARC, comprising administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.

71 – 79 (canceled)

80. (new): A compound having the structure:



wherein R^1 is selected from R, OR, NR_2, NHR, $NHSO_2R$ and $NRSO_2R$;

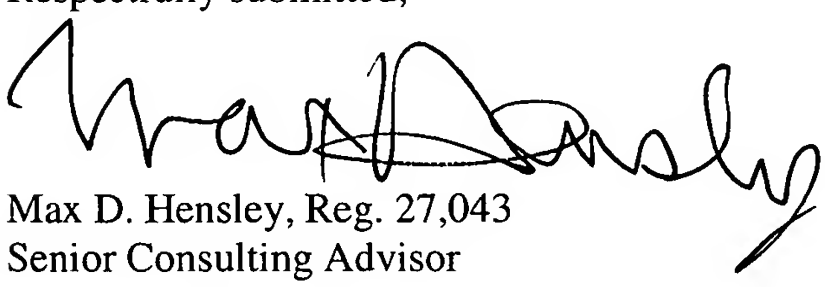
R^2, R^3 and R^4 are each independently selected from H, F, Cl, Br, I, OH, $-NH_2$, $-NH_3^+$, $-NHR$, $-NR_2$, $-NR_3^+$, C_1-C_8 alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C_1-C_8 alkylsulfonate, C_1-C_8 alkylamino, 4-dialkylaminopyridinium, C_1-C_8 alkylhydroxyl, C_1-C_8 alkylthiol, $-SO_2R$, $-SO_2Ar$, $-SOAr$, $-SAr$, $-SO_2NR_2$, $-SOR$, $-CO_2R$, $-C(=O)NR_2$, 5-7 membered ring lactam, 5-7 membered ring lactone, $-CN$, $-N_3$, $-NO_2$, C_1-C_8 alkoxy, C_1-C_8 trifluoroalkyl, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_3-C_{12} carbocycle, C_3-C_{12} substituted carbocycle, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

R is independently selected from H, C_1-C_8 alkyl, C_1-C_8 substituted alkyl, C_6-C_{20} aryl, C_6-C_{20} substituted aryl, C_2-C_{20} heteroaryl, and C_2-C_{20} substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof.

Applicants believe that the amendment is now compliant and that the claims are in condition for allowance. Applicants believe that no extension of term or other fees are required. If, however, any extension or fee is required, please charge Account No. 07-1250.

Respectfully submitted,



Max D. Hensley, Reg. 27,043
Senior Consulting Advisor

Date: 7/29/05